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THE
Journal of Obstetrics & Gynaecology
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VOL. 50, No. 4 NEW SERIES AUGUST, 1943

Phases of Maturation, Fertilization and Early Development in Man

BY

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INTRODUCTION.

AN account is given by Allen and others[1] of attempts that have been made in the past to secure human tubal ova. They recovered 5 ova by reverse irrigation of the uterine tubes from the uterus. An unfertilized ovum was recovered by Lewis[2] by flushing the uterine tube which had been previously removed with a myomatous uterus; two other ova were recovered by Pincus and Saunders.[3] Rock and Hertig[4] report the recovery of an unfertilized ovum, but do not give any details concerning it.

Until the publication by Dible and West,[5] and that by Hertig and Rock,[6] and more recently the account of young embryos given by Rock and Hertig,[4] the youngest human embryo was the "Miller" described by Miller[7] and Streeter[8]; unfortunately only 5 sections were preserved.

The present communication gives a description of an unfertilized ovum showing the second maturation spindle, an unsegmented ovum at an early stage of fertilization, and a young chorionic vesicle partially implanted in the endometrium.

DESCRIPTION.

The first specimen was obtained from a woman who was sterilized on account of severe mitral stenosis. The ovum was recovered by flushing the uterine tube after its removal on the 17th day of the menstrual cycle; ovulation probably occurred less than 12 hours before. The cycle previous to that from which the ovum was recovered was of 30 days duration. At the operation the right ovary showed a recently ruptured follicle with a small amount of blood still escaping. When examined in the fresh state the ovum was surrounded by several layers of corona radiata cells which were attached to a homogenous zona pellucida. (Plate I,

fig. 1.) The vitellus was yellowish in colour, uniformly finely granular and completely filled the zonal cavity. It did not show the three types of yolk bodies described by Lewis,[2] but resembled more closely the second ovum described by Pincus and Saunders.[3]

After fixation the ovum was found on histological section to be at the stage of the second maturation spindle. (Plate I, fig. 3.) The polar body showed scattered chromosomes in its cytoplasm. Dixon[9] concluded from an examination of an oöcyte in the ovary that the second maturation spindle was completed before the oöcyte left the ovary but the appearances found in this specimen and in the descriptions given by Allen and others[1] for two of their shed ova and by Pincus and Saunders[3] do not support Dixon's opinion. Whether the second maturation division is completed in the absence of fertilization cannot be stated at present.

The second specimen was obtained from a woman who was sterilized as her last 2 pregnancies terminated as miscarriages on account of severe toxaemia. Her menstrual cycles previously were of the 28 day type. The ovum was recovered by flushing the tube removed on the 16th day of the cycle; coitus had taken place 2 and 4 days previously. At the operation the ovary showed a recently ruptured follicle with some blood still escaping. When examined in the fresh state the ovum was found to be free of corona radiata cells. The zona pellucida appeared as a homogenous membrane in which many completed sperms were found. (Plate I, fig. 4.) The vitellus did not completely fill the zonal cavity; at one side there were a number of granules, probably remains of the polar bodies. The vitellus showed a clearer zone in the centre and its general appearance was that of early degeneration.

The third specimen (the "Barnes" embryo), an early chorionic vesicle partially implanted in the endometrium, was found after hysterectomy on the 25th day of the menstrual cycle. The patient had an ovarian cyst and was suffering from excessive menstrual loss. Coitus had taken place on the 10th and 12th days previous to the date of operation.

At the operation a considerable amount of free fluid was found in the peritoneal cavity. The left ovary contained a cyst about 4 inches in diameter and also a corpus luteum. The uterus was slightly enlarged and soft. As the nature of the ovarian cyst was in doubt a total hysterectomy, bilateral salpingectomy, and left oophorectomy was performed. The appendix was also removed.

The uterus was incised along the attachment of the broad ligament on each side and was then opened, separating the anterior and posterior walls from each other. The endometrium in the cervix and in the lower part of the body was hypertrophic and polypoidal. The endometrium lining the remainder of the uterine cavity appeared to be normal; it showed, in approximately the middle of the posterior wall, a small elevation which was just visible to the naked eye. On examination with a low power binocular microscope the elevation appeared as a slightly raised translucent area which was clearly demarcated from the surrounding endometrium. The elevation was tentatively diagnosed as a young implanting blastocyst or a retention cyst of a uterine gland.

After fixation with Bouin-Allen the area became opaque but was still raised above the level of the surrounding endometrium. (Plate II, fig. 5.) A block of the uterine wall containing the swelling was removed and after dehydration, clearing and double embedding was cut at 7μ. Microscopical examination of the sections showed

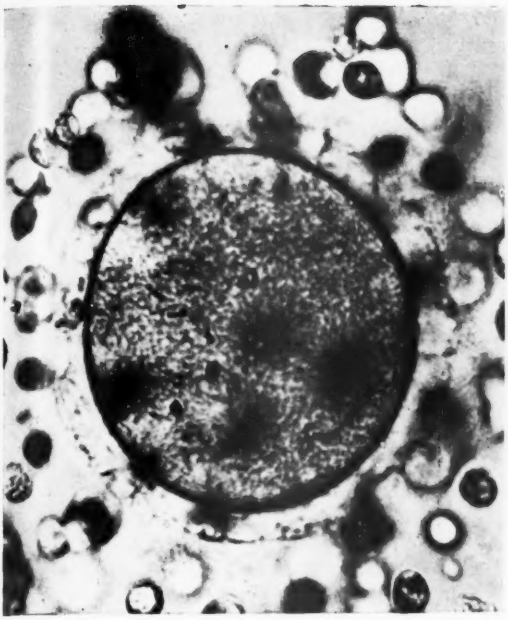

FIG. 1. Photomicrograph of ovum No. 1 in the living state. The dark areas on the vitellus are corona radiata cells on the upper or lower surface of the zona. × 480.

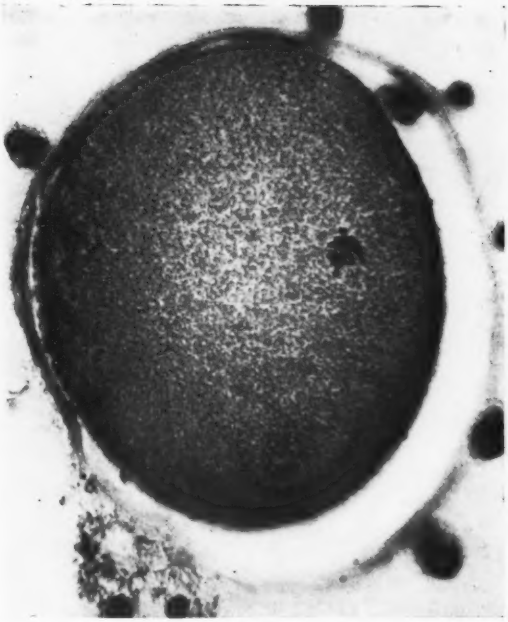

FIG. 3. A section of ovum No. 1 showing the metaphase of the second maturation division. The first polar body (out of focus in the upper right-hand corner) is seen. The vitellus has shrunk from the zona pellucida and most of the corona radiata cells have been lost. (cf. Pl. I, Fig. 1). × 820.

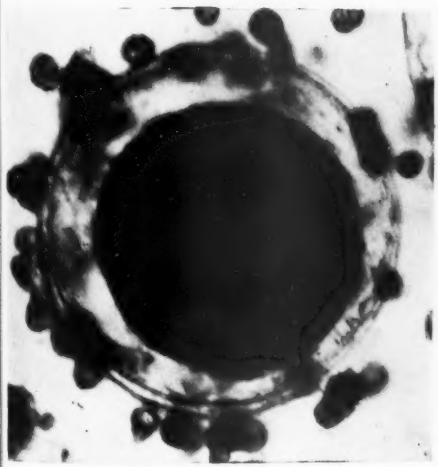

FIG. 2. The same ovum immediately after fixation. × 480.

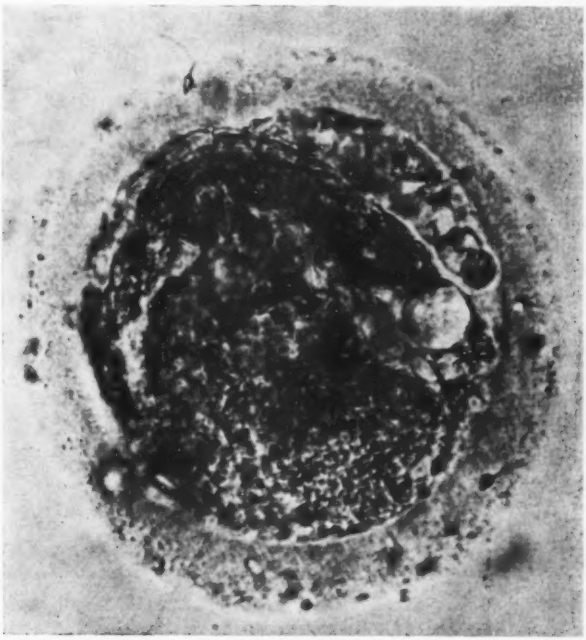

FIG. 4. Photomicrograph of ovum No. 2. A complete sperm is seen in the zona pellucida; other sperm heads are visible. At the upper right-hand corner of the photograph globular detritus is seen. × 480.

J.H.

FIG. 5. A surface view of the endometrium of specimen No. 3. The smooth elevation produced by the implanting embryo is seen. The endometrium shows fissures and crevices which for the most part are associated with the mouths of the uterine glands. × 15.

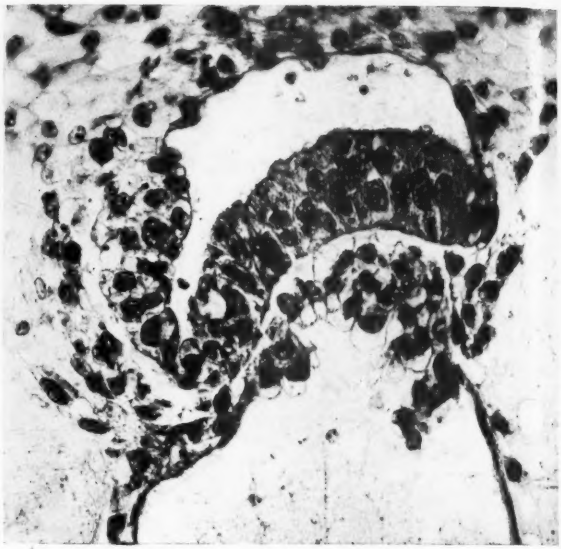

FIG. 6. A high power view of the embryonic disc showing the columnar nature of the embryonic ectoderm and the arrangement of the endoderm. The cells of the latter are continuous with Heuser's membrane. × 400.

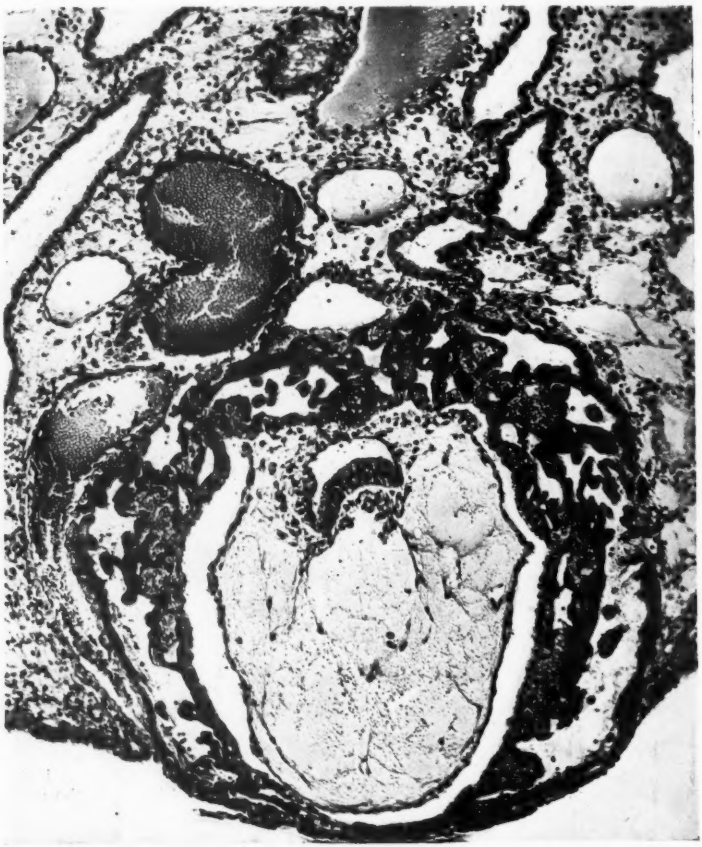

FIG. 7. A general low power view of the implanting embryo and surrounding endometrium. The latter is oedematous and in it there are many dilated blood vessels. The extent of the syncytiotrophoblast and cytotrophoblast in different parts of the vesicle is shown. The extra-embryonic mesoderm has been artificially separated from the cytotrophoblast except at the embryonic pole. The embryonic rudiment has differentiated into a columnar ectodermal layer, which at the edge of the embryonic disc is continuous with the embryonic ectoderm of the amnion and a mass of endodermal cells which with Heuser's membrane enclose a cavity, the primitive yolk sac. × 110.

W.J.H.

an early implanted blastocyst. (Plate II, fig. 7.) The chorionic vesicle is not completely implanted in the endometrium as part of the elevation that projects into the uterine lumen is not yet covered by the uterine epithelium. This relatively superficial position of the chorionic vesicle in the present specimen resembles closely that of "ovum" No. 7700 of Hertig and Rock.[6] The trophoblastic shell varies in thickness; it is thickest over the deep embryonic region of the vesicle and thinnest in the abembryonic region where the uterine epithelium is absent. The trophoblast is differentiated into a cytotrophoblast and a syncytiotrophoblast. The calculated dimensions of the vesicle are approximately 0.931 × 0.770 × 0.737 mm. In some areas the syncytiotrophoblast has destroyed the wall of the blood vessels, allowing the blood to escape to a slight extent into the intercommunicating lacunae of the syncytiotrophoblast. The general appearance resembles very closely those described and illustrated by Hertig and Rock.[6] The peripheral edge of the syncytiotrophoblast, however, seems to be more sharply demarcated from the endometrium than in their specimens Nos. 7699 and 7700 and resembles more closely the appearance in their specimen No. Re. 7950, Fig. 4 (1942). The cytotrophoblast is composed of cuboidal cells which in some situations have proliferated to form irregular masses which project into the syncytiotrophoblast; these projections are the forerunners of the primary villi.

The endometrial tissue shows marked oedema, but there is no evidence of a decidual reaction. The glands of the endometrium are dilated and tortuous. Their epithelium seems to be resistant, at this stage, to the action of the syncytiotrophoblast and the glands appear to be pressed aside by the expanding vesicle (cf. Streeter, 1926).

The embryonic disc is convex towards the amniotic cavity and is composed of tall columnar epithelial cells which are continuous at the periphery of the disc with the amniotic ectoderm. (Plate II, fig. 6.) This for the most part consists of a layer of flattened cells but in one situation these cells are cuboidal. The endoderm is composed of from one to several layers of large cuboidal cells with vacuoles in their cytoplasm. In the younger embryo No. 7699 described by Hertig and Rock the endodermal cells are heaped up to form a mass as many as three layers thick but in their other specimens the endoderm forms a single layer. An endodermal yolk sac has not yet been formed but a cavity lined with endodermal cells and flattened mesodermal cells (Heuser's, or exocoelomic, membrane) encloses a cavity (Fig. 7) which has been designated by Hertig and Rock[6] in their specimens as the exocoelomic space. In this cavity there is a precipitated coagulum. The outer aspect of the cells of Heuser's membrane is continuous with a mesenchymal reticulum which fills the trophoblastic vesicle except where it has become artificially separated from the cytotrophoblast.

Probable age of the specimen.

As already stated coitus occurred 12 and 10 days before the operation. The last menstrual period began on the 25th May and, assuming that the present cycle would have been of 28 days duration, the next period was due on the 22nd June. Coitus occurred on the 6th and 8th June, i.e., 16 and 14 days before the expected next period. The operation was performed on the 18th June. If ovulation occurs (see later) 14 ± 1 (i.e. 13 to 15) days before the next menstrual period then ovulation occurred on the 7th to 9th June. A comparison of the present specimen with those of Hertig and Rock shows that No. Wi

8004 which is estimated to be 9½ days old, is much less developed. The embryonic disc of No. 7699, estimated age 11 days, is less developed but the syncytiotrophoblast has invaded the endometrium more than has that in the present specimen. It seems probable that ovulation occurred at the earliest on the 7th—8th June, and that the fruitful coitus was that of the 6th June. The age of the embryo is thus estimated to be from 10 to 11 days, mean age 10½ days.

Time of Ovulation

On the time of ovulation in women there is now an extensive literature which has been reviewed by a number of investigators (Knaus,[10] Dickinson,[11] Latz and Reiner,[12] and others). The evidence which has been accumulated during the past few years from a number of different methods of investigation seems to show that ovulation is more closely related to the succeeding menstrual period than to the beginning of the preceding menstruation. Ogino[13] Pryde,[14] Smith,[15] and Latz and Reiner[12] base this assumption on their investigations on the so-called "safe period." Schroeder [16] and Shaw[17] deduce the time of ovulation from the examination of the endometrium and related corpora lutea, and conclude that it occurs at about the middle of the cycle. Rock and Hertig,[4] by comparing the ages of young embryos with the associated endometrial histology, conclude that ovulation occurs 13 to 15 days before the next menstruation.

It is thus presumed that ovulation occurs about 14 ± 1 days before the beginning of the next menstrual period. The day, however, cannot always be accurately predicted since there is some variation in the length of the menstrual cycle in individual women. Gunn and others[18] state that no cases were found which did not vary at least 2.75 days between the shortest and longest interval, and Haman[19] states that there was no instance of absolute regularity in his series. Further, Rock[20] has suggested that about 3 per cent of the women in his series of 88 cases do not ovulate regularly 13 to 15 days before the next menstrual period and, therefore, do not fit into the general pattern.

The recovery of ova at a definite period of the menstrual cycle gives the most reliable information on the time of ovulation. Specimen No. 1 of the present series which was presumed to be recently shed since it was surrounded by many corona radiata cells was recovered 14 days before the presumed beginning of the next menstrual cycle. Table I gives the estimated age of all ova described up to the present and the approximate day of their recovery in the cycle. There is some evidence from these few cases to show that the time of ovulation is more closely related to the beginning of the next menstruation than of the preceding one.

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TABLE I.

Ovum	Corona cells	Polar bodies	Day of cycle ovum recovered	Length of menstrual cycle	Presumed number of days between ovulation and onset of next cycle	Remarks
Allen and others						
1	Nil	2 (19μ)	15th	Not stated	—	Ovum lost
2	Present	1	15th	Not stated	—	Twins—one from each ovary
3	Partly dispersed	1	15th	Not stated	—	
4	Partly dispersed	1	16th	Not stated	—	
5	3 layers	–	14th	Not stated	—	
Lewis	Nil	–	22nd	Formerly 28 days, last 35	14–15	Ovum possibly 1 day old
Pincus and Saunders						
1	Nil	–	19th	28 days	12	Ovum possibly 2 days old
2	Nil	1	20th	26–30 days	9–13	Ovum possibly 2 days old
Present paper						
1	Present	1	17th	Formerly 28 days, last 30	14	Not more than 12 hours old
2	Nil	? Polar debris	16th	28 days	14–15	Ovum lost; possibly 1–2 days old

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Two Cases of Renal Failure Following Abortion

BY

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THE two cases here described occurred within 3 months of each other in the Redhill County Hospital, Surrey. The first patient was a woman of 31, who was known to have had some degree of toxaemia in her previous pregnancies and to have had a residual hypertension; her illness had a fatal termination. The second patient was a girl of 18 years, in her first pregnancy. She gave a history of a fall and symptoms suggested a concealed accidental haemorrhage. After a long illness she has been discharged convalescent.

CASE 1.

Mrs. D., aged 31. Married, 3 children (1931, 1933, 1936).

Previous history. No scarlet fever, no tonsillitis. Had been attended by her doctor in each of the previous confinements for "kidney trouble." In the last confinement there was marked albuminuria, and raised blood-pressure. Some months later the blood-pressure was 160/100. When seen by her doctor in February, 1942, she was 6 months pregnant and showed symptoms of severe toxaemia. She was given a note advising admission to hospital, but she delayed coming to hospital for 5 days.

Condition on admission, February 10th, 1942.

Complained of headache, misty vision and spots before her eyes. Chest: nil. Heart: apex beat 4½ inches out from mid-line, tachycardia. Abdomen: uterus the size of a 24 to 26 weeks pregnancy. Very slight pre-tibial oedema. Small retinal haemorrhages. Marked albuminuria. Blood-pressure 230/155.

Morphia gr. ¼ given, also 10 c.c. of 10 per cent magnesium sulphate given intravenously on admission.

February 11th, 1942. Refused to have induction of labour.

February 12th, 1942. Patient worse. Complained of inability to see; also of pain in the chest. Heart enlarged 4½ inches to the 6th interspace. Triple rhythm. Tachycardia. Marked dyspnoea: fine crepitations at bases of both lungs. Petechial rash and haemorrhages on legs and abdomen.

5.30 p.m. Artificial rupture of membranes after catheterization. Ten ounces of dark-brownish urine withdrawn. Blood was not confirmed.

10.20 p.m. Delivery of foetus (26 weeks).

February 13th, 1942; 2.50 a.m. Completion of 3rd stage of labour. During the day ¼ ounce of urine was secreted. Blood-pressure dropped to 100/85.

Intravenous drip commenced—10 per cent of glucose in distilled water with 2 per cent soda bicarbonate (2 ounces four-hourly). The drip was kept going more or less continuously for several days, in the hope of encouraging the kidneys to work, until oedema became marked. The blood-pressure rose gradually, as did also the blood-urea. Magnesium sulphate was introduced into the duodenum by means of a Ryle's tube when the patient was unable to take it by the mouth—this, together with enemas, was to encourage the elimination of fluid by the bowel. Linseed packs were applied to the kidney area. Heart stimulants were given, but the patient became gradually more oedematous, more irrational, finally comatose, and died on the 8th day after delivery.

The course of the illness; the change of blood-pressure, urine-urea, blood-urea, also the output of fluid, are shown on the accompanying chart.

Post-mortem findings.

Heart: Left ventricle hypertrophied, but not dilated. Valves normal.

Liver: Serous surface smooth. Cut surface appeared normal.

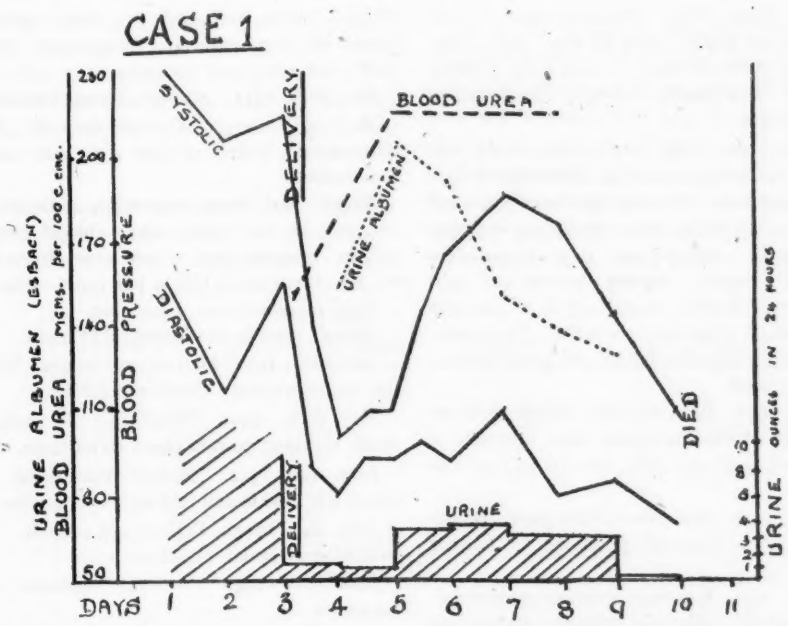

Chart showing blood-pressure, blood-urea, output of urine and urine albumin (Esbach).

Spleen: Hard—some fibrotic areas.

Blood vessels: No atheroma or sclerosis.

Kidneys: Large—subcapsular haemorrhages. Capsule peeled well.

Cut surface: Both kidneys showed complete bilateral cortical necrosis—very little normal substance seen. The whole of the cortex was greyish-white, with haemorrhages along the inner edge. There was a thin layer of more normal looking substance just under the capsule.

Ureters: Slightly dilated.

Uterus: Endometrium brownish and ragged. Placental site showed evidences of infection.

Section of kidney.

Section showed subacute nephritis, without evidence of chronic nephritis.

CASE 2.

Mrs. I, aged 18. Married. Primigravida. Emergency admission on May 15th, 1942, at 6 p.m.

Complained of vaginal haemorrhage and abdominal pain after a fall on the previous day. Pregnancy about 6 months.

Family history. Father died of pulmonary tuberculosis.

Previous illnesses. Rheumatism and chorea at 4 years of age. Scarlet fever at 8 years—in bed 14 weeks. Pleurisy at 16 years. Pleurodynia 8 months ago.

History of present condition.

May 14th, 1942. Fell down five steps and "split her legs." Took train home (8 miles). No discomfort that night.

May 15th, 1942. Attack of giddiness with backache when out in the morning. Walked home with help, and found that she had a small loss of blood. Doctor sent her into hospital.

Condition on admission.

Temperature 97.2°F. Pulse-rate 100. Respiration-rate 20. General condition good. Blood-pressure 95/68.

Uterus: Size of 26 weeks pregnancy. Marked contractions. Foetal heart not heard. Vertex presentation.

P.V. Cervix taken up—os not dilated.

May 16th, 1942. Abortion at 3 a.m. Complete 3.40 a.m. Foetus not macerated. Weight 2 pounds

8 ounces. Quiet day. Blood-pressure 90/68 8 p.m. Had not passed urine all day. 1 c.c. Carbachol given without result. 10.30 p.m. Patient catheterized. Ten ounces of deeply blood-stained urine withdrawn.

May 17th, 1942. Still not passing urine normally. On Catheterization the urine was deeply stained with blood. Morning specimen appeared to be almost pure blood; later specimens were less deeply stained. Intravenous drip gluco-saline commenced. Urinary deposit showed uric acid crystals, epithelial cells, an average of 16 pus cells and 1 red blood corpuscle per field. Casts were not seen. Gram negative bacilli and gram positive cocci were present.

May 18th, 1942. Blood-pressure rising. Still not passing urine. Urine contained large numbers of red blood cells and pus cells. One blood cast was seen.

May 19th, 1942. Condition fairly good. Blood-pressure 135/75. Linseed poultices to lumbar region.

May 20th, 1942. General condition maintained. Urine amphoteric, albumin present. (Guaiacum test for blood negative).

May 21st, 1942. Blood-pressure 145/98. Marked oedema of vulva and ankles. Right arm vein thrombosed. Urine alkaline. Many red blood corpuscles and pus cells, albumin present. Deposit showed epithelial cells, many red blood corpuscles and an average of 7 pus cells per field. Casts not seen. The culture was sterile. Seen by Professor Young. One pint of plasma given. Vein thrombosed.

May 22nd, 1942. Condition still fair. Blood-stained alkaline urine, albumin present, no sugar; deposit showed epithelial cells, red blood corpuscles and an average of 7 pus cells per field. Culture sterile. Temperature rose to 103°F. in the evening.

May 23rd, 1942. Condition deteriorating—oedema increasing. Vomited frequently during the day. One pint of plasma given, followed by one pint of blood. Swinging temperature up to 103°F. at night.

May 24th, 1942. Condition very grave. Right saphenous vein thrombosed and canula had to be withdrawn. Leg became very swollen and painful.

May 25th, 1942. Slight improvement in condition. Vulva and back still very oedematous. Right leg very painful. Temperature swinging. Left saphenous vein thrombosed.

May 26th, 1942. Marked diuresis established.

May 27th, 1942. Patient very ill. Diuresis maintained. Vulva, ankles and back still very oedematous.

Blood. Red blood corpuscles, 4,000,000; polymorphs, 89 per cent; white blood corpuscles, 35,400; lymphocytes, 9 per cent; haemoglobin, 80 per cent; eosinophils, 1 per cent; colour index, 1; large mononuclears, 1 per cent.

Patient restless and irrational at night.

May 28th, 1942. Diuresis 248 ounces. Very restless and irrational. Oedema subsiding.

May 29th, 1942. Complained of cough and of sharp stabbing pain in chest on left side.

June 1st, 1942. X-ray examination of the chest; left base is dull and shows congestion.

June 2nd, 1942. Patient not so well. Marked twitching of facial muscles.

June 3rd, 1942. General condition slightly improved.

June 6th, 1942. Impossible to obtain any samples of blood, because of immediate clotting of blood.

June 10th, 1942. White cell count, 9,400 per c.mm. Polymorphs, 62 per cent; lymphocytes, 37 per cent; eosinophils, none; basophils, none; large mononuclears, 1 per cent.

Relative lymphocytosis. Variation in size of red blood corpuscles. Normoblasts were present. Platelet count, 420,000 per c.mm. Coagulation time 5 minutes—time is diminished.

After June 6th, 1942, several attempts were made by Dr. Chamberlain and myself to obtain specimens of blood for blood-urea and other tests, but the blood clotted immediately in needles and syringe and in the veins—probably because of liver changes due to her toxic condition.

A sample was obtained on July 20th, 1942, but even then the veins thrombosed at the pricks, and we believe that there were further thromboses in the muscles, as there were contractures of both arms at the elbows and wrists. There were also contractures of the third and fourth digits of the left hand. These were treated by splinting and later by massage and exercises.

Thrombosis of the leg veins caused great diffi-

culty of movement, although gradual recovery took place, and the patient was able to get up at the beginning of August.

Her blood-urea was 35 mg./100 c.c. on July 20th, 1942, and 30 mg./100 c.c. on August 28th, 1942, and her urea concentration test became normal.

She was discharged on August 29th, 1942, her condition being very satisfactory, except for some residual contracture of the right elbow.

Urine	Blood-urea mg. 100 c.c. blood	Urine S.G.	Urine urea
May 19th, 1942	234	—	—
May 22nd, 1942	273	1.006	—
May 25th, 1942	356	1.009	0.5 per cent
May 27th, 1942	294	1.010	0.5 ,,
May 30th, 1942	192	1.010	1.3 ,,
June 3rd, 1942	—	—	1.3 ,,
June 6th, 1942	86	1.012	—
July 20th, 1942	35	—	2.0 ,,
July 27th, 1942	Urea concentration test (Before taking urea)		1.5 ,,
		(1 hour later)	2.3 ,,
		(2 hours later)	2.8 ,,
		(3 hours later)	3.2 ,,
Aug. 28th, 1942	30	—	—

The special interest of these 2 cases lies in the similarity of the sequence of clinical events.

Both patients were in the 6th month of pregnancy—after delivery there was a sudden alarming drop in blood-pressure indicating shock. There was haematuria (not confirmed in the first case) but very marked in the second case. This was followed by oliguria and a marked rise in the blood urea. In the fatal case the kidneys showed a complete bilateral cortical necrosis with sub-capsular haemorrhages—microscopically a sub-acute nephritis with no evidence of previous disease.

The first description of bilateral cortical necrosis was given by Juhel-Rénoy[1] in 1886, and in 1913 Rolleston[2] was only able to find 10 authentic cases in the literature. Almost all occurred in pregnancy, and all had a fatal termination.

In 1918 Clifford White[3] described 2 cases of puerperal anuria, in which he incised the renal capsule, and at the operation he removed a small portion of the kidney for section. His patients recovered, and from study of the sections he concluded that "the condition is an acute inflammatory swelling with oedema, which goes on to thrombosis and the necrosis which is found post-mortem." He considered that the suppression of the urine was due to the marked distension of the tubules and the space round the glomerulus; this causes stasis from which the patient may recover.

Crook[4] also incised the capsule in one of his patients with a satisfactory result, and in his sections found a focal necrosis in which the tubules were blocked with secretion and débris, the glomeruli also being necrosed.

Gibberd[5] in 1936 recorded 2 cases of patients recovering from accidental haemorrhage which had in each case been followed by oliguria (or anuria), and raised blood-urea, and described the kidney lesion as being due to engorgement of the blood vessels, followed by thrombosis and necrosis. Kellog[6] called attention to the frequency with which anuria and oliguria followed premature separation of the placenta and the great danger of this

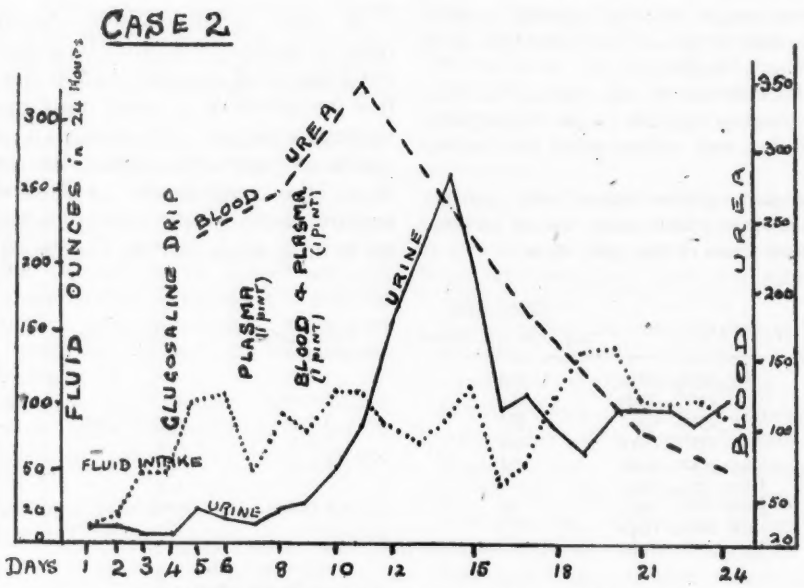

Chart showing intake of fluid, urinary output, and blood-urea.

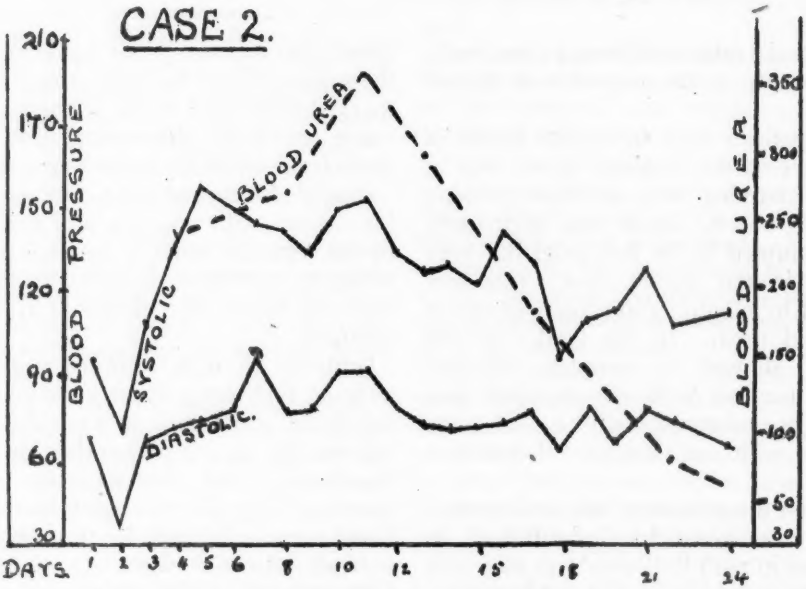

Chart showing blood-pressure and blood-urea.

occurring if the blood-pressure suddenly dropped.

In 1941 Lyman Duff and More[7] collected 71 cases of bilateral cortical necrosis with anuria and azotoemia described in the literature, including 42 surveyed by Ash[8] in 1933. The cases can be divided into 48 connected with pregnancy, and 23 not associated with pregnancy (including some males).

Of the pregnancy cases, two-thirds were associated with premature delivery, between the 5th and 8th months, or with a stillbirth. Twenty-one of the cases were associated with abruptio placentae and 8 with pre-eclamptic toxaemia.

Of the non-pregnancy cases, the majority were associated with severe infection,[1, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18] or with absorption of toxic substances.[16, 17, 18] Duff and More[7] give a detailed summary of the gross and microscopical descriptions of the affected kidneys.

(*a*) Areas of necrosis in the cortex, in which, although cortical tissue is clearly recognizable, all components are completely necrotic.

(*b*) A hyperaemic and haemorrhagic zone on the internal border of the necrotic areas with infiltration of neutrophils and extravasated blood cells.

(*c*) A thin layer of living tissue separating the area of necrosis from the capsule.

(*d*) Intra-vascular thrombi and intra-tubular casts.

As early as 1914, Professor James Young[19] put forward the view that a toxaemia of pregnancy evolves during the early stages of placental degeneration, and that the degree of toxaemia is in proportion to the placental lesion, which, in the early stages, is an ischoaemia of the tissue—also that by a consideration of the placenta an approximately correct antenatal history may be described.

In a recent paper[20] he suggests that many women, who have toxaemia in the later months, show an "abortion taint" in the early months, and that an increasing damage to placental tissue finally results in a pre-eclamptic toxaemia. A later recrudescence of bleeding (or accidental haemorrhage)—particularly if of the concealed type—by producing an extensive area of damaged tissue, which may involve uterine muscle—may result in anuria and azotaemia.

Delbet[21] has shown that damage to muscle tissue in severe wounds produces, in the early stages of absorption and disintegration, substances highly toxic to the organism. The concentration of these toxins, in excretion by the kidneys, probably initiates the damage to the renal tubules.

Further light on the aetiology of the kidney damage has been shed by the work of Bywaters and Beall[22] and others.[23, 24] They have defined the "crush syndrome," and have described the serious damage inflicted on the kidneys with 48 hours by excretion of bye-products of a severe crush injury of mesodermal tissues, i.e., severe shock frequently out of proportion to the apparent injury, followed by haematuria, oliguria (or anuria) and azotaemia due to damage of the renal tubules and the formation of casts in the lumen.

The pathological changes in the kidneys have been described in detail in a masterly paper by Bywaters and Delory[25] who give careful microscopical details of the condition. Professor J. Young[20] has pointed out the comparison that may be established between the condition of the kidneys in the "crush syndrome" and in accidental haemorrhage, and suggests that the aetiology is probably the same in each.

A similar picture has been drawn by Leslie Witts[26] and others[27, 28] of the

symptoms of the patient and the pathological condition of the kidneys in that outrage of mesodermal tissues—a mismatched blood transfusion.

Bratton[29] in the *Lancet* describes the microscopical appearance of kidneys of 9 cases of "anuria with casts," i.e. degeneration of tubules with necrosis of individual cells and formation of cellular casts (red blood cells, epithelial cells, leucocytes and blood pigment) with interstitial oedema and foci of sub-acute inflammatory infiltration. Blood vessels were engorged. Seven of these cases were described as "septic abortion" or "abortion with septic spleen," and had a history of anuria (or oliguria) and/or raised blood-urea. The case records given do not show when sepsis began, nor its relation to the anuria, but in the second case described above, the sepsis only appeared on the 7th day, when there was some slight recovery of kidney function. That is, the sepsis here seemed to be merely a complication of the original illness.

A second complication of the illness was a tendency to thrombosis with lowering of the blood coagulation time—a complication noted also by Gibberd.[5] In the account of his treatment of his cases Gibberd used 5 per cent intravenous glucose saline with 50 c.c. of 30 per cent glucose solution every 4 hours, but "due to the injection of the strong glucose solution" it soon became increasingly difficult to find a vein, as there was so much localized thrombosis. Davidson and Turner[30] particularly noticed thrombosis of the renal arteries in two of their cases, and suggest that a study of the coagulation time of the blood in these cases might be profitable.

A third interesting case has occurred recently in the wards, in which a damaged placenta was retained *in utero* for some hours with a resulting marked rise in the blood-urea.

The patient, aged 27, was delivered of her first baby in a nursing home. She had had a normal labour and delivery under a short chloroform anaesthesia. Delivery was at 6.15 p.m. At 7.15 p.m. as the placenta had not been delivered, the patient was given 5 units of pitocin and 0.5 mg. of ergometrine at 8 p.m. At 10.15 p.m. she was seen by a specialist. He found her in a state of severe collapse and a vaginal examination disclosed that there was a contraction ring below the placenta. He advised immediate admission to hospital.

On admission the patient was found to be in a state of severe shock and collapse. She was cold, restless, with a rapid thready pulse, which at times was almost imperceptible. The blood-pressure was 80/60.

On abdominal examination the uterus was felt to be almost stony hard, tightly contracted, tender, and lying over to the right. On vaginal examination neither the placenta or cord were felt, the cervix was soft, but the uterine muscle was tightly contracted above.

Shock treatment was given—morphia, 1 pint of plasma, 1 pint of blood.

Sept. 26th, 1942. At 1 a.m. blood-pressure 75/56; at 8 a.m. blood-pressure 110/40; at 2 p.m. blood-pressure 110/70; at 8 p.m. blood-pressure 130/90.

At 3 p.m. the placenta was removed manually under deep chloroform anaesthesia, was adherent in the right cornu, and was very ragged and came out in pieces.

Patient's condition rapidly improved, and a record was kept of intake and output of fluids, but a normal balance was instituted on the first day.

Sept. 26th, 1942. Blood-urea 79 mg./100 c.c. (before delivery of placenta).

Sept. 26th, 1942. Plasma potassium 21.8 mg./100 c.c. Blood-pressure 135/85—remained at this level through the week.

Sept. 28th, 1942. Blood-urea 53 mg./100 c.c. Clotting time 3 minutes 50 seconds.

Oct. 1st, 1942. Blood-urea 42 mg./100 c.c.

Oct. 12th, 1942. Patient greatly improved, only the pulse-rate remained in region of 110–120. Blood-urea 35 mg./100 c.c. Blood-pressure 130/80. Urine: the deposit contained urates, epithelial cells and some pus cells.

SUMMARY.

(1) Two cases are described of oliguria following abortion.

Case one: Patient with severe pre-eclamptic toxaemia, in whom the added trauma of induced delivery brought about shock and kidney disfunction.

Case two: A patient who fell, and probably had a traumatic accidental haemorrhage, which produced haematuria, shock and oliguria with azotaemia.

(2) A survey of recent literature indicates that possibly a common aetiology of the conditions may lie in a damaged placenta.

(3) Two noteworthy complications have been described.

(4) A third case is described, in which injudicious use of oxytocic substances caused the uterine muscle to contract tightly on a partly-adherent placenta, causing severe shock with marked rise in blood-urea.

I am indebted to Mr. Norman Pitt for permission to publish these cases, and to Professor Young for his valuable advice.

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Reactions to Pressor Substances in Normal and Toxaemic Women

BY

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IN 1937 Shockaert and Lambillon[1] published the results obtained by intravenous injection of a pressor substance, tonephin (an extract of the posterior pituitary lobe) in normal women not pregnant, and normal pregnant and puerperal women, and in women who had pre-eclamptic toxaemia. In normal women who are not pregnant an average rise of 45 mm. Hg occurred in the systolic arterial blood-pressure. In normal pregnant women in the last 3 months the corresponding rise was 13 mm. Hg, while in patients who had pre-eclamptic toxaemia it was 55 mm. Hg. At the same time there were general reactions on the part of the patients to the injections which differed considerablyin the 3 groups. In the women not pregnant the phenomena were very severe. Some seconds after the injection extreme pallor was noted and the lips were cyanosed; respiration was accelerated, there was dyspnoea and at the same time the patient had an indefinable sense of malaise, followed by nausea and even vomiting, and abdominal pains, with desire to empty the bowels or to pass urine. There were often cold sweats with small feeble pulse. These phenomena lasted for 7 or 8 minutes and then gradually passed away. In the normal pregnant women they were much less severe and might be almost entirely absent, and those that were present disappeared quickly—usually in 2 or 3 minutes.

From these observations Shockaert and Lambillon argued that there must be present in the serum of the normal pregnant woman, especially in the later weeks of pregnancy, some substance antagonistic to tonephin. In pre-eclamptic toxaemia, though such a marked rise occurred in the systolic blood-pressure the general reaction was less severe than in the women not pregnant but more severe than in the normal pregnant woman. In the puerperium they found that the refractoriness to tonephin, that had characterized the normal pregnant woman, disappeared rapidly so that by the 9th day of the puerperium the rise of blood-pressure and the general reactions were similar to those obtained in the normal woman not pregnant. The mean rise of systolic blood-pressure in normal puerperal women was 44 mm. Hg, i.e. practically the same as that in the normal woman not pregnant.

In the same year Dieckmann and Michel[2] published the results obtained by subcutaneous injection of pituitrin in 16 normal and 19 toxaemic women. In the former an average rise in the systolic pressure of 11 mm. Hg was obtained, while in pre-eclamptic toxaemia the average rise was 51 mm. Hg. From this high rise in pre-eclamptic toxaemia and also from the fact that the injection caused a marked decrease in the volume of urine they argued that the posterior lobe of the pituitary had something to do with the causation of the disease. Too much secretion may be produced or there may be some defect in its neutralization, or the woman might be

unduly susceptible to its action. In "vascular renal disease" in pregnancy the reaction obtained was similar to that in the normal pregnant woman, viz., 7 mm. Hg, and they therefore suggested the test as a means of differentiating this condition from pre-eclamptic toxaemia.

In 1938 de Valera and Kellar[3] published the results of tonephin injections in a similar variety of cases to those studied by Shockaert and Lambillon. Their results were on the whole very similar. For purposes of comparison the three sets of results are shown in Table I.

The comparable figures obtained by the author are given in column 4.

more or less frequent intervals until the base level was reached. This took from 30 to 45 minutes. The pulse-rate at this time was also recorded. Tonephin (Bayer) 0.66 c.c. was then injected slowly into an arm vein. Systolic and diastolic blood-pressures were then recorded at first at intervals of 30 seconds or thereabouts, and later less frequently until the base level was again reached. The time taken to reach the base level was noted. Throughout the experiment the objective reactions were noted, including the pulse-rate and after it the patient was questioned regarding her sensations. In addition, therefore, to notes of the general reaction records were

TABLE I.

Reactions to Pressor Substances (Rise of Systolic Arterial Pressure in mm. Hg) in Normal and Toxaemic Women.

(Comparative Results of Various Workers).

	Shockaert and Lambillon (Tonephin)	Dieckmann and Michel (Pituitrin)	de Valera and Kellar (Tonephin)	Browne (Tonephin)
Normal women not pregnant ...	45	—	35	21.3
Normal pregnant women ...	13	11	23	33.2
Pre-eclamptic toxaemia ...	55	51	43	54
Pregnancy with chronic hypertension	16*	7.7	—	.53
Normal puerperal	44	—	44	48.2

* It is doubtful whether these are the same kind of case that I classify as "hypertensive." Shockaert calls them *femme brightique*. Possibly they are examples of chronic glomerular nephritis.

It will be seen that while the figures are in most respects similar there are certain important differences. In view of these it was decided to repeat the experiments and that to eliminate so far as possible the personal factor they should all be done by one worker (myself). The method used was as follows: The subject, at a time as far distant from her last meal as possible, was placed recumbent on a couch or bed. After a short period of rest her blood-pressure was taken and the estimation repeated at

obtained of the rise of systolic and diastolic blood-pressures and of the time taken for their return to normal. In a certain proportion of all except the puerperal patients cold pressor tests (by putting the hand and forearm in an ice bath) were also carried out for purposes of comparison. Finally in many of the patients tonephin tests were repeated in the puerperium—in some two or three times. As the experiments have occupied the last 2½ years they extended over the worst periods of the air attacks

on London, and as many of the women were evacuated to distant places in the country prolonged follow-up in the puerperium was often impossible. As will be seen later the reactions of these patients in the puerperium offer an interesting and possibly a fruitful field for investigation.

The results of the tests including the mean rises of systolic and diastolic blood-pressure, standard deviations (S.D.), range, and time taken to return to normal levels are shown in Tables II to VI.

obtained. The mean systolic rise was 21.3 mm. Hg. (Table II.)

Normal pregnant women (20 cases). Most were at term or near it and none was under 35 weeks. All were healthy before pregnancy, none had albuminuria or oedema at any time and the highest blood-pressure reached during pregnancy had not exceeded 130/70. The mean systolic rise was 33.2 mm. Hg. (Table III.)

Pre-eclamptic toxaemia (20 cases). Full details of these, including the signs of

TABLE II.

Summary of Reactions to Tonephin and Cold Pressor Tests in Normal Pregnant Women. (24 cases).

(Reactions are in mm. Hg and the time in minutes).

	Mean rise in systolic blood pressure	S.D.	Mean range	Mean rise in diastolic blood-pressure	S.D.	Mean range	Mean time till normal
Tonephin tests (24 cases) ...	21.3	9	3–37	24.3	9	10–45	5.6
Cold tests (8 cases)	21	7.4	10–32	21.7	6.2	10–30	7.5

TABLE III.

Summary of Reactions to Tonephin and Cold Pressor Tests in Normal Pregnant Women and in their Puerperium (20 cases).

(Reactions are in mm. Hg and the time in minutes).

	Mean rise in systolic blood-pressure	S.D.	Mean range	Mean rise in diastolic blood-pressure	S.D.	Mean range	Mean time till normal
Tonephin tests (20 cases) (Pregnancy) ...	33.2	13.3	7–60	20	7.9	0–30	8
Cold tests (10 cases) (Pregnancy)	23.1	8.6	9–44	20.5	7.3	7–30	5.5
Tonephin tests (3 cases) (Puerperium) ...	49	10.8	32–58	39	5.5	34–45	6.5

The most important results may be summarized as follows.

Normal women not pregnant (24 cases). All these were healthy young women in their early twenties who had never been pregnant. In each case the day of the menstrual cycle on which the test was made was noted but this did not seem to have any constant or striking effect on the result

toxaemia present, are shown in Table VII, which also shows the reactions obtained by the cold pressor tests in a number of cases and the results of further tonephin tests in the puerperium. The mean systolic rise during pregnancy was 54 mm. Hg. (Table IV.) In many cases the rise is maintained in the puerperium.

Pregnancy with chronic hypertension

TABLE IV.

Summary of Reactions to Tonephin and Cold Pressor Tests in Pre-eclamptic Toxaemia and in their Puerperium (20 cases).

(Reactions are in mm. Hg and the time in minutes).

	Mean rise in systolic blood-pressure	S.D.	Mean range	Mean rise in diastolic blood-pressure	S.D.	Mean range	Mean time till normal
Tonephin tests (20 cases) (Pregnancy) ...	54	19.1	12–79	38.1	18.3	12–79	11.5+
Cold tests (9 cases) (Pregnancy)	19.2	10.4	4–40	19.7	13.2	0–48	8
Tonephin tests (14 tests on 10 patients). (Puerperium)	52.8	15.3	30–86	36.7	12.4	10–60	12

TABLE V.

Summary of Reactions to Tonephin Tests in Normal Puerperal Women (20 cases).

(Reactions are in mm. Hg and the time in minutes).

Mean day of puerperium	Mean range	Mean rise in systolic blood-pressure	S.D.	Mean range	Mean rise in diastolic blood-pressure	S.D.	Mean range	Mean time till normal
10	5–20	48.2	10.75	32–68	42.4	10.2	20–60	10 +

TABLE VI.

Summary of Reactions to Tonephin and Cold Pressor Tests in Pregnant Women with Chronic Hypertension and in their Puerperium (8 tests on 7 patients).

(Reactions are in mm. Hg and the time in minutes).

	Mean rise in systolic blood-pressure	S.D.	Mean range	Mean rise in diastolic blood-pressure	S.D.	Mean range	Mean time till normal
Tonephin tests (8 cases) (Pregnancy) ...	53	11.4	30–62	25	9.9	14–40	11
Cold tests (6 cases) Pregnancy	46.1	9.9	27–55	21.7	10	12–42	8
Tonephin tests (3 cases) (Puerperium) ...	60	10	48–75	36	12.4	20–60	6.5

(8 tests on 7 patients). In these patients chronic hypertension had existed before pregnancy. There are few patients in this series partly because they are somewhat scarce, but partly also because it was not considered fair to carry out the test on some of the worst cases lest the life of the foetus might be endangered. The mean systolic rise was 53 mm. Hg. (Table VI.)

Normal puerperal women (20 cases). None of these had suffered from pre-eclamptic or any other form of toxaemia during pregnancy and the blood-pressure had not, at any antenatal examination, exceeded 130/70. The day of the puerperium on which the test was done varied from the 5th to the 17th and the average was 10. The mean systolic rise was 48.2 mm. Hg. (Table V.)

Discussion.

It will be seen that the results differ materially from those obtained by Shockaert and Lambillon. One of the most striking differences is in the increases of systolic pressure in normal women not pregnant, and normal pregnant women. Evidence was not found of the presence of any inhibitory substance such as was predicated by these authors, and by de Valera and Kellar. Indeed the systolic rise in the normal pregnant woman is significantly greater than in the normal woman not pregnant. Does this mean that some sensitizing substance is present in normal pregnancy that is absent in the nullipara? If this is so one naturally thinks of the experiments of Byrom[4] who produced lesions in albino rats closely resembling those of eclampsia, by injecting vaso-pressin. He also found that the sensitivity of the rat to vaso-pressin could be increased tenfold by preliminary treatment with oestrogenic hormone, and that in unspayed rats the sensitization could equally well be brought about by gonadotropic hormone.

All the workers including the author are agreed as to the great and significant increase in systolic pressure obtained in pre-eclamptic toxaemia. A reference to Table VII will show that it occurred in almost every case. Regarding the cause of it one can again only speculate and again Byrom's experiments are suggestive. Smith and Smith claim to have found an increase of prolan in pre-eclamptic toxaemia but their results have been severely criticized by Taylor and Scadron[5] who did not find any constant increase. Taylor and Scadron however agree that oestrin is diminished in toxaemias. It might also be suggested that in women who suffer from pre-eclamptic toxaemia there is a personal or familial predisposition to hypertension and hence to hypersensitiveness to pressor substances. This was strongly suggested by the results of cold pressor tests carried out by the author and published in 1940.[6] If it is so it is remarkable that no such high reaction occurred in any of the 24 normal young nulliparae on whom tests were done.

It is of great interest to note that the high reactions to tonephin in patients with pre-eclamptic toxaemia are maintained in the puerperium. Whether this is a permanent change is not yet known. In one of the patients (see Table VII) it had diminished considerably by the 52nd day of the puerperium but in another it was still present on the 235th day—the longest time that any one of these patients has so far been followed up. It may be that it is a hypersensitivity characteristic of patients with chronic hypertension or of women who will later in life develop hypertension. The latter explanation seems to be untenable in view of the fact already mentioned that none of the 24 normal young nulliparae gave a very high reaction. According to Robinson and Brucer[7, 8] 40 per cent of the population are actual or potential hypertensives, i.e. will, if they survive, and apart altogether from pregnancy, develop hypertension. It is somewhat unlikely, therefore, that not one of these women is a potential hypersentive.

The high reactions obtained in the puerperia of women who had had normal pregnancies are also very striking. The mean systolic rise of 48.2 is significantly greater than those found in normal pregnancy and much greater still than those in the normal nulliparae not pregnant. It will be noted however (Table I) that only slightly lower values for the normal puerperium were obtained by Shockaert and Lambillon and by de Valera and Kellar. The cause of this increased sensitivity after delivery is not known, nor how long it lasts. In one case it was still present on the 20th day of the puerperium and in two others

TABLE VII.

PRE-ECLAMPTIC TOXAEMIA

Reactions to Tonephin and Cold Tests in Pr

				TONEPHIN TEST				COLD TEST			
No.	Age	Parity	Weeks pregnant	Basic blood-pressure mm. Hg	Systolic rise mm. Hg	Diastolic rise mm. Hg	Time till normal in minutes	Basic blood-pressure mm. Hg	Systolic rise mm. Hg	Diastolic rise mm. Hg	Time norma minu
1	22	0	39	115/78	79	42	10	115/78	25	12	10
2	30	0	37	104/60	44	30	12	100/60	20	10	3
3	25	0	40	128/70	52	30	9·5	128/70	4	0	1
4	21	0	40	118/70	32	20	13+	118/70	14	10	3
5	22	0	35	130/54	70	46	13				
6	32	0	35	118/75	12	0	10				
7	23	0	40	120/75	75	85	11+				
8	22	0	36	135/75	75	40	17				
9	33	0	37	128/80	72	30	11				
10	26	1	39	94/44	24	26	7				
11	21	0	36	128/50	72	50	?	130/40	30	48	7
12	26	0	32	152/70	62	40	14+	150/70	40	40	10
13	27	0	34					180/70	10	20	15
14	25	0	32	150/70	50	30	8	148/80	12	20	15
15	28	1	40	110/40	65	60	11+	114/58	18	17	4
16	39	1	40	150/86	55	24	14+				
17	24	1	36	85/50	65	20	9·5				
18	26	0	40	116/60	64	55	14				
19	32	1	28	78/35	52	?	?				
20	28	0	38	124/60	48	60	8				
21	25	0	38	128/78	20	37	4·5				

VII.

OXAEMIA (21 Cases).

ts in Pregnancy and the Puerperium

ic Hg	Time till normal in minutes	Puerperial Tonephin Test: Day of puerperium	Basic blood-pressure mm. Hg	Systolic rise mm. Hg	Diastolic rise mm. Hg	Time till normal in minutes	Evidence of pre-eclamptic toxaemia	Remarks
	10	10	114/70	86	30	10.5	B.P. 155/98. Alb. +	
	3·75	10	104/56	48	39	9+	B.P. 140/90. Alb. 0	
		52	100/50	35	40	8.5		
	1.5	11	122/65	43	40	13+	B.P. 154/100. Alb. + Oedema +	
	3·5	8	90/45	40	35	5·5	B.P. 140/96. Alb. + Oedema +	
		12	130/70	60	40	19+	B.P. 160/100. Alb. + Oedema + +	
							B.P. 140/98. Alb. + + Oedema + +	Twin pregnancy
							Eclamptic. B.P. 168/112 Alb. + Oedema +	
							B.P. 150/90. Alb. + Oedema +	
		7	130/70	70	40	10	B.P. 154/108. Alb. + +	
							Alb. on one occasion only in pregnancy. Oedema in both feet. B.P. normal.	Pyelitis in last pregnancy. Possibly not toxaemic.
	7						B.P. 140/80. Alb. + Oedema +	
	10	9	130/60	75	60	14+	B.P. 215/140. Alb. +	Foetal heart sounds irregular after tonephin injection. Marked spasm of arteries of fundus oculi and convulsive foetal movements—Recovered.
	15+						B.P. 202/110. Alb. +	Twin pregnancy. Tonephin tests not proceeded with.
	15+	12	144/70	56	50	16+	B.P. 190/140. Alb. +	
	4·25						B.P. 142/90. Alb. + ?	
		13	108/65	50	15	10	B.P. 198/90. Oedema + Alb. +	
		60	112/65	58	45	14+		
		235	110/60	48	40	22+		
		8	100/58	40	30	16+	B.P. 132/100. Oedema + + (legs face and hands)	Intrauterine death of foetus. (*Not* a result of tonephin)
		55	94/50	30	10	4		
							B.P. 160/100. Oedema + +	
							B.P. 152/78. Oedema +	
							B.P. 143/90. Gross Oedema. Alb. +	
							B.P. 154/102 No alb.	

on the 17th day. Withdrawal of progestin after delivery might be suggested but work has not yet been done to prove or disprove this view and Byrom found that the sensitization in rats caused by oestrogenic substances could not be prevented by progesterone.

It will be noted (Tables IV and VI) that the mean systolic rise with Tonephin was similar in pre-eclamptic patients and in those with chronic hypertension in pregnancy, and that both were very high, but that the reactions to the cold test were different. In pre-eclamptic toxaemia the reaction to the cold test was low (mean systolic rise 19.2 mm. Hg) while in the chronic hypertensives it was high (46.1 mm. Hg). It is possible, therefore, that the cold test might be of value in differentiating these two conditions.

Shockaert and Lambillon laid great emphasis on the differences in the general reactions obtained in the various groups, especially in supporting their view that an inhibitory substance was present in normal pregnancy which was absent in the non-pregnant. In the present series the reactions were very variable and unpredictable, and as the changes caused were mostly subjective (pallor, faintness, cold sweats, pulse slowed or rapid and weak, numbness, abdominal pains, headaches, etc.) they could rarely be accurately measured. The general reaction often seemed to bear little or no relation to the amount of elevation of the blood-pressure.

Summary and Conclusions.

1. This paper deals with the results of tonephin injections and cold pressor tests in a series of healthy nulliparae not pregnant, normal pregnant women, normal puerperal and toxaemic women.

2. Evidence has not been found of the presence of an inhibitory (antipressor) substance in normal pregnant women. Rather does it appear that a sensitizing substance may be present in normal pregnancy that makes the patient more sensitive to pressor substances than the non-pregnant woman.

3. The pre-eclamptic patient is much more sensitive to the action of pressor substances than either the normal non-pregnant or the normal pregnant woman. Some of the possible reasons for this are discussed.

4. A similar hypersensitivity is present in the patients with chronic hypertension in pregnancy, i.e. patients in whom chronic hypertension existed before pregnancy.

5. The hypersensitivity characteristic of the patients with pre-eclamptic toxaemia continues in the puerperium and has been found as late as its 235th day. Whether it is permanent or not is not known, neither is it known if it is universal.

6. The same hypersensitivity is present in the normal puerperal woman who has had a normal (non-toxaemic) pregnancy. This has been found as late as the 20th day of the puerperium.

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Delivery of the Foetal Head in Occipito-Anterior Positions of the Vertex

BY

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SPEAKING in Manchester some 10 years ago, the late Professor Blair Bell, after referring regretfully to the fact that so many women died as a result of childbearing, declared "Since these deaths are tragedies where there should be rejoicing in the consummation of a natural event, it comes about that even though the mother escape with her life . . . this happy issue is liable to obscure subsequent disabilities which persist, sometimes to "dog her footsteps" for life. It is the urgent, the dramatic, that affects: the long-drawn-out is too often regarded as inevitable—a pleasing alternative to "something worse." "The woman damaged by childbirth" (to quote Professor James Young) is a constant reminder of our shortcomings in maternity practice, and of the urgent need for redoubled efforts to reduce the incidence of maternal disablement, and my study has been undertaken with this object in view. Again in the words of Blair Bell "There is ample room for improvement among the most proficient, and this is related chiefly to perfection of technique and the application of correct procedure, all of which require thought, and then further thinking."

THE MECHANISM OF LABOUR.

Owing to the comparatively small size of the birth canal in relation to that of the mature foetal head, it is apparent that all sectional planes of the head will not readily pass through the canal, and that some process of adaptation or accommodation will be necessary before the birth of the child can take place. The series of movements which facilitate the passage of the foetus through the maternal canal and the mechanical factors responsible for their occurrence are referred to as the mechanism of labour. A knowledge of certain anatomical facts about the parturient canal and the foetal head is essential to a full understanding of this mechanism and its practical application to the management of labour.

The genital tract in the non-pregnant state may be looked upon as a potential elastic channel which will not be completely opened until the largest disengaging plane of the foetal presenting part is lying in the vaginal orifice. During pregnancy the uterus enlarges progressively and, in the course of labour, the lower uterine segment is expanded and the cervix, vagina and vaginal orifice are dilated as the foetus is advanced. When the vagina is distended, the perineum is depressed, elongated and broadened, the anus is dilated and the anterior segment of the obstetrical perineum, between the posterior labial commissure and the anterior anal margin, is greatly thinned and stretched, its muscles being displaced posteriorly and laterally. The posterior ano-coccygeal segment of the perineum is also under tension and the

coccyx is extended. The expanded parturient canal, the passage through which the foetus must be driven during birth, may therefore be described as a cylindrical canal, circular in cross-section and curved on the antero-posterior plane. Only its upper half lies within the bony pelvic cavity. Its anterior internal surface is short and convex, its posterior internal surface is long and concave, and its axis is a curved central line corresponding with the axis of the pelvis in its upper and a continuation of this curved line in its lower segment.

The cavity of the true pelvis in the living subject is upholstered with muscles which also assist the aponeurotic, fascial and neuro-vascular structures to close the interosseous spaces. This muscular layer reduces the available diameters of the basin and helps to convert it into the rigid cylindrical channel through which the upper part of the parturient canal passes. The suspensory and supporting structures of the pelvic diaphragm, of which the most important in relation to our study are the superficial fibro-muscular and cutaneous tissues of the anatomical perineum, the musculature of the pelvic floor, and the pelvic fasciae, bridge and almost close the pelvic outlet.

The anatomical perineum, which includes all those structures covering the pelvic outlet, may be divided into the urogenital and anal triangles. These have a common base on the bis-ischial diameter, which crosses the perineum immediately in front of the anus. The obstetrical perineum lies between the posterior labial commissure and the coccyx. Beneath the cutaneous tissues of the urogenital triangle are the superficial perineal muscles, the rigid uro-genital diaphragm and its contents which are pierced by the urethra and vagina, the former, thickened by the presence of its intrinsic sphincter in its upper third, lying in close relation to the anterior vaginal wall. The bulbo-cavernosus acts as a sphincter for the vaginal orifice, the sphincter urethrae membranacae compresses the urethra, and the transverse perineal muscles fix the central tendinous point of the perineum. In the anal triangle lie the anal canal with its sphincters and the fibro-fatty supporting tissues of the ischio-rectal space.

The muscular layer of the pelvic floor consists of the levator ani, the coccygeus (ischio-coccygeus) and the pyriformis on either side and, apart from the urogenital aperture between the levatores ani in front closes the pelvic outlet. Each levator ani consists of two parts, the ilio-coccygeus, which arises chiefly from the lateral pelvic wall at or near the white line to be inserted into the lower sacrum and coccyx and supports the pelvic and abdominal viscera, and the pubo-coccygeus, which arises from the back of the pubis and anterior part of the white line, forms the lateral margin of the uro-genital aperture, and is inserted into the perineal body, the ano-coccygeal raphe, and the coccyx. Its anterior fibres, of which only a small number pass in front of the anal canal to the central point of the perineum, form the pubo-rectalis muscle which acts as a powerful sphincter for the urogenital aperture. During the 2nd stage of labour the pubo-rectalis encircles the lower part of the parturient canal in the pubo-anal plane, its anterior fibres having maintained their normal relation to the bis-ischial diameter.

The deep intra-abdominal fascia, which lines the muscular and bony walls of the abdomen and pelvis, splits into three layers at the origin of the levator ani on either side. One descends caudally to line the lateral wall of the ischio-rectal space, the second covers the inferior surface and the third the superior surface of the levatores ani and coccygei muscles. The endo-pelvic fascia is in continuation with the sub-peritoneal tissue and overlies the deep fascia

above the levatores ani. It is a loosely woven connective tissue which covers the upper aspect of the pelvic floor and invests the pelvic viscera not covered by peritoneum above this level. Condensations of this fascia develop in lines of stress, usually in relation to blood vessels, to give additional support to the viscera. The most important of these are the anterior and lateral true ligaments of the bladder, the post-vesical fascia, the transverse cervical ligaments, the utero-sacral ligaments and the rectal fascia. The anterior true ligaments of the bladder constitute, with the post-vesical fascia, the pubo-cervical fascia. These condensations have a considerable admixture of elastic and muscular tissue, giving them a resilience and contractility which aids their supporting function.

The foetal head may be looked upon as a solid semi-paraboloid body with a plastic vault and rigid base, the latter being joined by the flexible neck to the trunk. Its size is variable, but the following table will give the average dimensions in inches of the more important planes of the unmoulded skull of a 7-pound foetus together with a concept of their relative sizes:

PLANES OF FOETAL SKULL.

Name	Diameters	Circumference	Area
Sub-occipito-bregmatic	3¾ × 3¾	12¾	9
Sub-occipito-frontal	4 × 3¾	13	11¾
Occipito-frontal	4½ × 3¾	13½	13¼
Occipito-mental	4½ × 3¾	13½	13¼
Vertico-mental	5½ × 3¾	14½	16¼
Sub-mento-vertical	4 × 3¾	13	11¾
Sub-occipito-mental	3¾ × 3¼	12¼	6

During its propulsion through the maternal passages in the course of labour, the foetal head is subjected to compression by the resistant and resilient walls of the parturient canal and this effects a certain alteration in the shape of the vault of the foetal skull which is brought about by a hinge-like movement and overriding of the bones at the sutures, and possibly by a minor reduction in size of the skull by expression of small quantities of cerebro-spinal fluid and of venous blood from the cranial cavity. The brain itself is incompressible but the medulla may sometimes be depressed into the foramen magnum. The degree of moulding is proportional to the constraining force to which the head is subjected and its resistance to compression primarily depending upon the degree of ossification of the cranial bones and the strength of the dural septa. When the tenacity of the dural septa is exceeded, rupture occurs and there is a considerable risk of intra-cranial haemorrhage. As the diameters of the engaging plane of the foetal head are shortened there is a compensatory lengthening of the diameter corresponding with the axis of that plane and which lies in the axis of the birth canal. Thus the vertico-mental diameter is elongated when the sub-occipito-bregmatic plane is engaging, the sub-mento-vertical diameter when the occipito-frontal plane is engaging, and the sub-occipito-bregmatic diameter when the vertico-mental plane is engaging.

A secondary modification in shape of the foetal head is caused by the development of the caput succedaneum on the leading unsupported part of the scalp due to pressure during uterine contractions against a relatively indistensible ring, the dilating

cervix in the case of the primary caput and the vaginal canal or ostium for the secondary caput. Either or both may be enlarged in cases of prolonged or obstructed labour, according to the level of the arrest of the head in the birth canal.

In occipito-anterior positions of the vertex the flexed foetal head is driven into the birth canal during labour as the lower uterine segment is expanded and the cervix is withdrawn. The longitudinal diameter of engagement, with the occiput to the front usually occupies one or other of the oblique diameters of the pelvic brim but may sometimes enter its transverse diameter. Flexion normally increases during early descent of the head and the sub-occipito-bregmatic sectional plane is brought into the normal sectional planes of the birth canal at the various levels of the girdle of contact. Deflexion results in the engagement of larger planes, thus the occipito-frontal is 47 per cent and the vertico-mental 80 per cent greater in area than the sub-occipito-bregmatic plane. The bladder is usually elevated with the lower uterine segment into the abdomen. During the second stage the foetal head advances within the vagina with each contraction and recedes during relaxation, and in addition the vaginal wall at the girdle of contact and in advance of the foetal head is driven down during the contraction and returns to its original position in the interval of rest. The major axis of the foetal head, at right angles to the plane of engagement, tends to pass into the axis of the parturient canal. When these axes correspond, resistance to further progress is minimal. This movement, considered in relation to the antero-posterior diameters of the canal, constitutes internal rotation, and, in relation to the transverse diameters, extension of the foetal head. Internal rotation and primary (pre-crowning) extension of the foetal head may therefore be looked upon as different aspects of a single movement designed to bring the major axis of the foetal head into that of the birth canal.

Internal rotation of the foetal head through one-eighth or one-quarter of a circle brings the occiput beneath the sub-pubic arch, and results from the operation of a number of interrelated factors. It is most likely to take place when the uterine propulsive force is adequate; the birth canal will dilate to form an intact curved cylindrical channel; the foetal passenger is proportionate to the maternal passage, which will offer adequate elastic resistance to its descent; the foetal head is well flexed at an early stage of labour, moulded in this attitude of flexion and capped by a caput succedaneum to convert it into a semi-paraboloid form with a flexible attachment at the neck to the cylindrical trunk; lateral inclination is easier than further flexion of the already fully flexed head, which tends to extend and reoccupy a position of rest in relation to the trunk. Deflexion of the head results in angulation between the head and trunk which converts the forepart of the foetus into an asymmetrical body convex anteriorly and concave posteriorly, a shape which facilitates the completion of its internal rotation and progress through the lower curve of the birth canal. Conversely rotation is likely to be delayed and incomplete in the presence of uterine inertia, perineal deficiency, a small foetus and a spacious, atonic birth canal, incomplete flexion, premature extension, non-moulding or abnormal moulding of the foetal head, and foetal atony or rigor mortis due to intra-uterine death Under favourable conditions, primary extension of the head commences in cases of occipito-posterior position as soon as the occiput rotates in front of the transverse diameter of the pelvis, and therefore as soon as internal rotation commences in

cases of occipito-anterior position. At first the amount of extension is slight, but as internal rotation is nearing completion the movement is greater, and it ceases when the mento-vertical axis of the head corresponds with the axis of the birth canal. This primary extension of the head is brought about by extension of the cervical spine as a whole and, unlike secondary extension, is not a simple hinge-like movement at the atlanto-occipital joint. The head is deflexed, the vertex is thrust forwards towards the vaginal outlet, the cervical spine is opposed to the posterior surface of the pubes and the occiput is freed beneath the pubic arch. If primary extension did not take place and complete flexion was maintained, delivery could be effected only by direct advance of the foetal head through the centre of the pelvic floor, the head being unable to negotiate the curve of the birth canal.

As the presenting part advances the obstetrical perineum is expanded, the anus becomes turgid and dilates to expose a D-shaped area of the anterior wall of the anal canal, and the vaginal orifice, the least distensible part of the vaginal canal, is gradually stretched. The scalp overlying the postero-medial angles of the parietal bones first appears at the vaginal orifice and, as the head is crowned, the occiput is freed beneath the pubic arch and the anterior part of the vertex distends the anterior margin of the perineum, which is markedly thinned. A small posterior laceration of the fourchette which usually bleeds freely may be considered inevitable in primiparae at this stage. The sub-occipital region, between the superior nuchal lines and the posterior margin of the foramen magnum becomes fixed below the pubic rami as the distended perineum resists further caudal descent of the vertex, and the head begins to pivot around the sub-occipital point. This is the mid-point of the sub-occipital region which lies in contact with the anterior margin of the vaginal orifice and below the symphysis pubis and represents the nearest accessible point to the atlanto-occipital joint. The urethra lies in the triangular recess bounded by the medial borders of the pubes and the sub-occipital region of the foetal skull and therefore escapes damage. The frontal and facial regions pass over the perineum in turn to complete the birth of the head, the disengaging planes being the sub-occipito-bregmatic, sub-occipito-frontal and sub-occipito-mental. Secondary extension is brought about by the removal of the resistance to ascent of the free occiput after crowning, when caudal pressure causes the frontal end of the head lever to descend, and by the resultant force of the *vis a tergo* of the uterus and the reactionary force of the perineum driving the head forwards and upwards. If the vaginal outlet is inadequate in size to permit the passage of the disengaging head or secondary extension commences before the occiput is born, laceration of the perineum and posterior vaginal wall may result, these parts being more vulnerable than the anterior vaginal wall as the long posterior concave wall of the birth canal lies in the direct line of force through the advancing foetus. The risk of laceration is increased when the sub-pubic angle is acute and the head is necessarily displaced backwards towards the coccyx, and of damage to the attached muscles and ligaments when the coccyx is over-extended. Premature extension of the head would increase the area of the largest disengaging plane by 13 per cent, the occipito-frontal replacing the sub-occipito-frontal plane.

The Management of Labour.

The purpose of assistance at delivery of the foetal head is to aid the series of move-

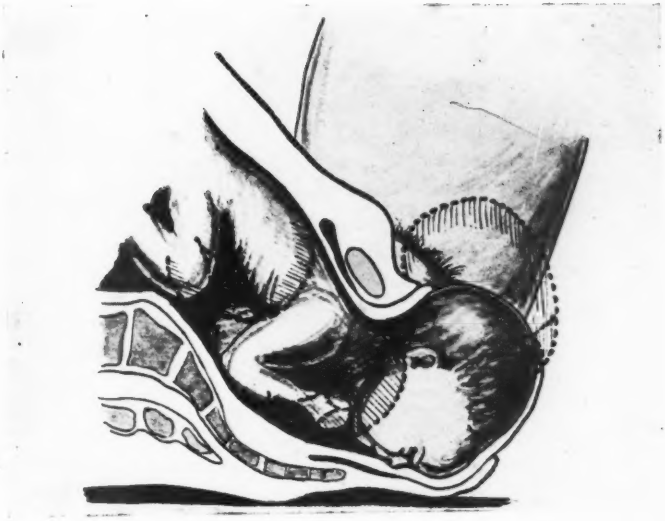

FIG. 1.
Diagrammatic representation of the progress of the foetal head through the birth canal. (Adapted from Ten Teachers Midwifery.)

FIG. 2.
Birth of the foetal head showing the disengaging diameter before the occiput has been freed from the vestibule.
(Adapted from Stander and Williams.)

W.H.

FIG. 3.
Birth of the foetal head showing the disengaging diameter after the occiput has been freed from the vestibule.
(Adapted from Stander and Williams.)

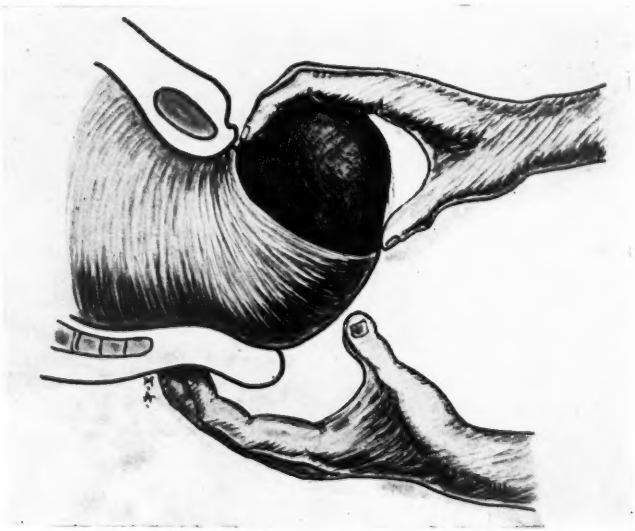

FIG. 4.
Completion of the forward thrust of the foetal head in primary extension aided by ano-coccygeal pressure. (Adapted from Bumm.)

FIG. 5.
A case of stress incontinence of urine showing a healed anterior vaginal laceration and an intact perineum.

W.H.

ments which constitute the mechanism most favourable to the successful termination of labour with minimal damage to the mother and child.

The choice of position for the patient during the second stage of labour is of some importance. Probably the most satisfactory attitude to adopt before the presenting part appears at the vulva is the exaggerated lithotomy position, the patient grasping the knees of her flexed and widely separated legs and straining as at stool during pains. This is inferior only to the squatting position as a means of using the accessory powers to best advantage and has the additional merits that it is less trying to both patient and attendant than the majority of the alternative attitudes. She should not tense her adductor or pelvic floor muscles, as this may delay the advance of the foetal head and increase the risk of damage both to the pelvic floor and to the intra-cranial structures, and she should rest with her feet on the bed between contractions. In occasional cases, if the patient is nervous and rigid, local perineal anaesthesia may assist relaxation and co-operation may be rendered more satisfactory. As soon as the presenting part appears at the vaginal orifice the patient is put into the position chosen for delivery, the bladder having previously been emptied.

The chief considerations in the choice of suitable delivery position are practicability, accessibility, relief of perineal tension and non-interference with the normal course of labour. Thus Sims' position is unsuitable owing to the difficulty in maintaining asepsis and control of the patient, the squatting position is impracticable owing to the inaccessibility of the parts, to increased perineal tension, and to anaesthetic difficulties, and the exaggerated lithotomy position owing to increase of perineal tension due to leg flexion. The two most satisfactory and convenient positions for delivery are the dorsal position with the legs semi-flexed and the knees apart, and the left lateral position with the right leg raised and semi-flexed and the left leg straight or nearly so. In the former the work of the assistant is less arduous and the patient need not be moved immediately after delivery, but the perineum is less accessible, the hand extending the head through the perineum is more liable to be contaminated from a soiled bed and, at a later stage, there is less freedom of movement for delivery of the anterior shoulder. In the latter, an assistant is fully occupied in supporting the left leg and, in domiciliary practice, the only assistant is usually required to devote all her full attention to the administration of the anaesthetic at this stage. The choice between these two positions usually depends upon the circumstances of the specific case under consideration.

The attendant should now stand at the right side of the bed facing the vulva. Both hands should be free, and the practice of passing the left arm around the right thigh of a patient lying in the left lateral position is to be condemned as the observance of strict asepsis is embarrassed, the control of the head before and during delivery is unsatisfactory, and withdrawal of the hand is necessary as soon as the head is born for the toilet of the eyes and upper respiratory passages, and for delivery of the shoulders and trunk. The patient takes a deep breath and, fixing the diaphragm and grasping the bed, a sling attached to the foot of the bed, or the hands of an assistant, bears down strongly and repeatedly so long as the pain lasts. Three or four sustained "bearing-down efforts" will effect a much more satisfactory advance of the head than multiple, brief, spasmodic attempts to strain. Co-operation is usually assisted by the judicious use of light, inter-

mittent anaesthesia, and the patient should rest between contractions.

The use of vaginal lubricants is not recommended when the foetal head has reached the pelvic floor, but a small quantity of undiluted Dettol or Dettol cream is usually put on the fingers before necessary vaginal examinations during the course of labour and this may help to reduce the delaying effects of friction upon the advancing head. Lubricants applied in advanced labour render the grasp by the hands of the attendant on the foetal head less secure and its control more difficult. As the perineum is expanded and the head is crowning the fingers of the right hand should be placed behind the occiput and the thumb near to the anterior fontanelle in order that the risk of a rapid, uncontrolled, surprise advance of the head, with its attendant risk of laceration of the perineum, may be obviated. A sufficient degree of flexion should be maintained to keep the axis of the foetal head in that of the lower strait of the vagina. When in doubt about the degree of flexion which should be effected, it may be useful to remember that premature extension is usually more harmful at this stage than delayed extension, and therefore it is wise to err on the side of over- rather than under-flexion. When necessary, completion of internal rotation may be assisted by gentle manual rotation of the flexed head between contractions to carry the anterior fontanelle towards the posterior vaginal wall and holding it in that position until the next contraction fixes it. This manoeuvre is usually unnecessary when adequate time is allowed for perineal distension, but in certain cases may materially assist the progress of labour.

As the occiput is disengaged from the pubic rami it should be freed from the anterior margin of the vaginal orifice by displacing the vestibule and labia minora to the nape of the neck. In a well moulded or dolicocephalic head, and, to a lesser degree, in a normal unmoulded head, this will expose a considerably greater area of scalp in the occipital region, will bring disengaging planes of smaller area through the vaginal orifice, will reduce the risk of damage to the anterior vaginal wall, the uro-genital diaphragm, and its contents, including those responsible for urinary control, and will relieve perineal tension. Manual "ironing" of the perineum is more liable to cause trauma than natural distension by the foetal head and increases the risk of concealed laceration of the perineal body. When necessary, if the uterus is contracting powerfully, the advance of the head may be retarded to allow gradual stretching of the perineum to occur by inducing the patient to refrain from violent bearing down efforts, the careful use of general anaesthesia and support of the exposed vertex by the right hand. Pressure on the head through the perineum greater than is necessary to maintain adequate flexion may increase the risk of damage to the pelvic floor and is therefore unsuitable for restraining the head. No true "support" is afforded to the perineum by direct pressure, except by retarding the advance of the head, therefore it is more reasonable to support the head by pressure on the scalp itself rather than on a vulnerable medium already under tension. In no case should labour be obstructed by preventing advance of the foetal head without lessening the *vis a tergo* from a powerfully contracting uterus by general anaesthesia. If a uterus is contracting strongly the force directed against the perineum is less when the patient is in the left lateral than in the supine position so the former is more suitable when contractions are too powerful, and vice versa. Howat states that the head should advance about half an inch with each pain as the perineum begins to stretch and about one quarter of an inch

when the head is crowned. This may be taken as a guide to the progress which may be considered satisfactory. If the second stage of labour is unduly prolonged the cumulative effect of repeated advance and retreat of the foetal head may result in permanent overstretching of the vaginal wall and its subjacent structures, especially the urethra and its sphincters. Further, the lower vagina is normally softened by venous congestion and may become oedematous and more susceptible to trauma in prolonged labour. As the head advances the occiput is again freed from the vestibule and the bi-parietal, the longest disengaging transverse diameter, escapes from the vaginal orifice as secondary extension commences. At this stage the foetal brow may usually be palpated through the ano-coccygeal segment of the perineum, and the head may be fixed in its position of maximal descent by pressure of the fingers of the left hand, palmar surface forwards, in this region during a contraction and held in that position until the uterus relaxes. This pressure will also complete the forward thrust of the foetal head which accompanies primary extension. As soon as this fixation has been achieved the patient should stop bearing down, and breathe deeply as she is anaesthetized. Delivery should never be attempted when the patient is semi-anaesthetized as she may suddenly strain, force the inadequately controlled head through the vaginal orifice and lacerate the perineum unnecessarily. With full anaesthesia, when the power of a contraction is waning or spent and control of the head is most complete, extension may be initiated by forward displacement of the brow and later of the upper jaw and sometimes the chin, by manipulation through the perineum by the fingers of the left hand, the vertex still being steadied by the right hand as the frontal region slowly passes over the posterior labial commisure. The right hand is now rotated on the foetal head until the temples can be grasped transversely and the head is slowly and deliberately extended by drawing forward the bi-temporal diameter, the perineal skin, now under reduced tension, being grasped laterally and drawn forwards and towards the mid-line by the fingers and thumb of the left hand as the irregular face is freed from the posterior labial commissure, to minimize the risk of tearing or extending a laceration of the perineum. The perineum must not be drawn back over the extending brow and face as this would increase tension and the risk of laceration. When necessary an assistant may aid the birth of the head by pressing on the foetal breech through the uterine fundus. Finally a finger is passed behind one angle of the jaw and swept under the chin to the other side to free the mandible and complete the delivery of the head.

If the size of the vaginal outlet is inadequate for the passage of the foetal head during the second stage of labour or laceration of the perineum and posterior vaginal wall is imminent, one or more of the following signs may be evident:

1. Arrested progress of the 2nd stage of labour with the head resting on the perineum in spite of powerful uterine contractions and good co-operation on the part of the patient.
2. Depression of the perineum is not accompanied by dilatation of the vaginal orifice and the sub-pubic angle is acute.
3. Formation of a firm indistensible ring within the vaginal orifice.
4. Laceration of the lower third of the posterior vaginal wall before the perineum is fully expanded.
5. Blanching of the perineum as the head descends during uterine contractions.
6. "Beading" of the perineal skin with serum.

7. The appearance of multiple minute perineal fissures which tend to bleed.

8. Progressive enlargement of a secondary caput succedaneum on the foetal scalp at the vaginal orifice.

If such a state arises there are five possible courses open to the attendant. Labour may be allowed to proceed and the perineum to rupture, its extent being modified only by the skilful and correct control of the foetal head during delivery; an attempt may be made to limit extension of the laceration by pressure on a broad area of perineum, by inserting perineal sutures under graduated tension (Wright) or by a deep transverse incision of the perineal body (Howat); or the laceration may be forestalled by deliberate incision of the perineum. The first two courses involve a considerable risk of severe perineal laceration and foetal intra-cranial trauma and the third may cause perineal mutilation through stitches "cutting out," may damage the foetal face during delivery and, if used for subsequent reconstitution of the perineum as originally recommended, will not effect a satisfactory repair. Transverse incision of the perineum intended to prevent spread of a commencing perineal tear is a method of treatment which, although it is based on sound arguments and may, in a number of cases, limit the spread of laceration, has important disadvantages. Spontaneous rupture of a resistant perineum carries a significant risk of intra-cranial injury to the foetus, a laceration once started extends rapidly and may have spread too far before the check incision can be made, the hands at this stage are fully occupied in controlling the movements of the foetal head, especially as the resistance to its descent is suddenly removed by perineal rupture, and therefore the time cannot be considered opportune for a cautious and careful transverse incision of a body which has neighbours of consequence. Further, in favourable cases a deep T-shaped wound involving the full thickness of the perineal body, including the superficial perineal muscles and anterior retractile fibres of the pubo-rectalis is difficult to repair efficiently and, if extension does occur, the difficulty is increased by the formation of a deep stellate laciniate wound. None of these methods afford any protection to the anterior vaginal wall or the subjacent urethral sphincters, and labour is unnecessarily prolonged.

When the laceration is inevitable or the advance of the foetal head is delayed by rigidity of the vaginal orifice, deliberate division of the perineum with scissors, if performed with prudence, will prevent unnecessary suffering by shortening the 2nd stage of labour, will minimize the risk of overstretching or tearing of the anterior vaginal wall, the muscular contents of the urogenital diaphragm, the anal sphincter and canal, and the rectal fascia and wall and will lower the forceps rate. It will also facilitate subsequent perineal repair by leaving a clear-cut surgical incision in a preselected position instead of an irregular laciniate wound and will reduce the hazard of intra-cranial trauma. This operation of episiotomy, referred to by von Oettingen as active protection of the perineum, should be delayed whenever practicable until the perineum is under tension so that the deeper structures will be displaced from the line of the incision. The patient should be lightly anaesthetized unless a local anaesthetic has previously been injected.

If the head cannot be fixed in its position of maximal descent by the fingers opposed to the ano-coccygeal region assisted by pressure on the uterine fundus, the perineum should be stretched laterally and firmly depressed by the separated index and second fingers of the left hand introduced into the vagina while the incision is being made. This digital stretching must,

however, be considered inferior to expansion by the advancing foetal head.

The choice of incision is of considerable importance. A lateral incision gives little increase in available space, there is some possibility of inflicting damage on branches of the internal pudental artery, and unequal retraction of the wound edges with deep recoil of the divided levator fibres renders apposition and repair difficult. A median, posterior incision gives a maximal increase in available space with little irreparable damage to underlying structures, straightforward repair with a minimal amount of tension on wound edges and satisfactory healing in nearly all cases, its only disadvantage being the risk of laceration of the anal sphincters and canal if extension occurs. This risk may be obviated by converting it into an L-shaped incision, the lower limb of which passes through the tissues antero-lateral to the anal sphincter. Such an incision will divide the skin, subcutaneous tissue, superficial transversus perinei and bulbo-cavernosus muscles, the urogenital diaphragm and deep transverse perineal muscles, a few anterior fibres of the pubo-rectalis and the lower part of the posterior vaginal wall. The anal sphincters and canal, and the rectal fascia and wall are undamaged. The postero-lateral incision is intermediate in advantage and disadvantage between the posterior and lateral incisions. Bilateral postero-lateral incisions are to be condemned as the increase in available space at the vaginal outlet is no greater than that obtained by a single posterior incision, while the centre flap retracts, is difficult to suture in position and, after repair, usually forms an atrophic, inefficient perineum consisting of little more than vaginal mucosa and perineal skin. A timely episiotomy, if properly performed and efficiently sutured, will therefore conserve the integrity of the maternal tissues, assist involution of the lower birth canal, prevent disorders of micturition and defaecation, and reduce the risk of traumatic intra-cranial lesions in the child, especially when premature. Overzealous care of the perineum at the expense of the anterior vaginal wall and apparatus concerned with urinary control is to be deprecated.

After episiotomy the foetal head should be delivered with care to prevent extension of the wound, special attention being directed to the completion of internal rotation, the maintenance of adequate flexion until the occiput is born, the displacement of the vestibule to the nape of the neck before secondary extension is permitted, and slow delivery of the head. Forceps delivery is necessary in only a small proportion of cases after episiotomy. It is occasionally permissible to give an intramuscular injection not exceeding $2\frac{1}{2}$ units of posterior pituitary extract after episiotomy if uterine contractions are feeble but not spasmodic, labour has not been prolonged, the membranes have not been ruptured for more than 3 hours, internal rotation is complete, an area of foetal scalp not less than 2 inches in diameter shows at the vulva during uterine contractions, the pubic angle is obtuse and there is no disproportion between the foetal head and the maternal bony and soft tissues. This treatment is unjustifiable when there is disproportion even of minor degree, when the membranes have been ruptured for some hours and spasmodic uterine contraction or contraction ring may be present, and when the vertex does not adequately expand the perineum during contractions.

In conclusion it should be stressed that every effort should be made to encourage the mechanism of delivery least liable to damage mother and child, meddlesome midwifery should be deprecated but conservatism should not be construed to mean inaction, and a decision as to whether any

particular line of treatment should be labelled conservative or impetuous should be based upon the after-history and findings at postnatal examination rather than upon a consideration of immediate technique. The importance of postnatal examination as a means of assessing results cannot be overstressed.

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A Further Study of the Clinical and Pathological Properties of Malignancy

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IN 1941 there appeared in the *American Journal of Gynecology and Obstetrics* (Vol. xliii, 210–220) a paper entitled "Ovarian Malignancy." In it, the opinion was propounded that malignancy, of whatsoever kind, is a disease in which a single cell of the body, in favourable circumstances, begins to proliferate under a certain internal stimulus and, by its multiplication, its daughter cells develop into a local growth; that all the cells of that growth, whether near or remote, are descendants of that parent cell; and that the malignant stimulus might affect two or more cells of different function and morphology somewhat simultaneously in different parts of the body.

The truth of those statements, I felt at the time, needed further factual elucidation. Let us deal with these clauses seriatim; first, the theory of the single cell proliferation.

It has been my good fortune, in the course of routine microscopy, to stumble upon several cases of extremely early malignancy of the female genital tract. One of these was found in the endometrium, 7 in the cervical canal, and 1 in the medulla of the ovary. The endometrial malignancy was clinically unsuspected, of course. It involved a microscopic part of the mucosa and extended in a cylinder-fashion from the surface down two-thirds of the depth of the mucosa. If one can judge of malignancy by the microscope, then this was malignancy. It was clean-cut, with sharply defined margins from the normal mucosa on either side of it, and there was not a sign of papillary outgrowth in the surface, or of circumstantial reaction. At the margin of the growth malignant cells, clearly defined by a different protoplasm and different nuclear arrangement, lay side by side with normal endometrial cells. These latter seemed to be quite unconscious of an enemy in their midst. There was not the slightest sign of transition from the normal to the malignant type. The change was abrupt and clean, but the internal milieu of these two cells was as different as the characters of a peaceful citizen and a gangster.

In the early carcinoma of the cervix, the same seemingly inoffensive beginning of malignant newgrowth also was found. Here, however, there were certain enlightening discoveries. Not only was the growth clearly delineated from the normal cells, but certain glandular tubules, cut transversely, showed malignant cells affecting only a segment of the lining epithelium, while the rest of the circumference was lined by normal cervical mucosa cells. This delineation in minute ducts was found very frequently, and in them there was not a vestige of transition from one type of cell to the other. I have found that transitional types occur only when inflammatory reaction disturbs both types—the malignant and the non-malignant cells. The margins in the specimens were as clear-cut as social distinctions. Here in this region, where the chief function of the lining cervical mucosa would seem to be to secrete a downward flow of thick quasi-impervious mucus to protect the uterine mucosa from invasion,

it was noticeable that the malignant cells were devoid of that chief function, and this cell energizing seemed to spend itself, not in functional activity, but wholly in division. We can assume that, as the body is the composite picture of all its component cells and as the human body is limited to the energy it can expend at any given time, that energy can dispel itself in any one way to its full capacity, but not in more than one way to that same degree. So it would seem that division and function are maintained in an inverse ratio. It is generally conceded that when a normal cell is in a state of division, its chief normal function is temporarily abrogated, not only until the division has been completed, but also until the newly-born daughter-cells have grown to a state to initiate their own function. Then function goes on in a crescendo until full maturity requires reproduction to renew the youth of the cell. Malignant cells never seem to reach maturity before division again interrupts development. The same rules apply to the individual. It is conceded, and has been frequently expressed in literature, that the normal woman's cerebral creative ability is abrogated during pregnancy. It has been stated that a woman in her pregnant state has never produced anything noteworthy, other than a child. And, like cells after kariokenesis, the child's functions during intrauterine aquatic life and in the terrestial stages of living are in a state of progressive functional capacity until maturity. So it would seem that the inference is justifiable that the highest functions of cells are first lost in malignancy and that this deprivation of function is progressive until all cell energy is consumed in a speed-up of cell division.

The microscopic newgrowth in the ovary was, of course, discovered only at biopsy. It was exceptionally small microscopically, as stated above, and was a malignant papilliferous growth. It undoubtedly was malignant from its inception, because it was malignant throughout. What the structure was, in which the growth took its origin, could not be determined.

All the above-quoted cases show quite clearly that malignancy has something which other non-malignant cells do not possess, and that that property of heightened cell-division is transmissable from cell to cell only through parent cell to daughter cells, and not by propinquity or even contiguity, for we have seen that seemingly normal cells, so far as we can judge by morphology and staining properties, can carry on normally, while juxtaposed against 'cells presenting all the hall-marks of malignancy. If this be true, then the clinical inference is clear-cut, that though certain tumours of the ovary may be looked upon as being prone to malignancy, yet we must conclude that those tumours are malignant or benign from their inception, and if a large ovarian tumour is benign in its greater mass, and shows malignancy at one spot, that malignancy is an accidental after-development brought about by a new chain of circumstances which has affected one or more susceptible cells.

These mixed types of ovarian tumours are preponderantly of the pseudomucinous types, which are now looked upon as teratoid tumours, in which the endoblastic element is the dominant type of growth; and the reason why this form of ovarian newgrowth is prone to carcinomatous development (not change) lies probably in the fact that endoblastic carcinomatous growths greatly outnumber ectoblastic epithelial cancers. The carcinomatous types arise chiefly in columnar epithelial surfaces and areas covered by so-called transitional epithelium. These are the easily vulnerable internal surfaces of the body, compared with the imbricated

epithelial coverings of the body's exterior. For that same reason teratoid tumours and teratomata of the ovary are prone to heightened division to the state which we designate as malignant.

Malignancy, however, both clinically and pathologically is a purely relative term. But what exactly do we mean by that statement? It admits of several interpretations. There are tumours which clinically are malignant, but by microscopic criteria are benign, and the reverse is equally true. That there are no hall-marks whereby pathologists can distinguish between malignancy and non-malignancy is shown by the fact that cautious pathologists nowadays will not venture a diagnosis without a knowledge of the clinical history. In other words, a prognosis from a pathologist, like that of a clinician, is based upon a review of the course of that and similar cases. Experience has taught caution in such cases, and experience is the main guide to the value of any such judgment.

The susceptibility of the patient is behind the progress of any malignant newgrowth. Local malignancy may be developed by the assistance of an abnormal local dysfunction, such as chronic infection or other trauma, in a patient who has no susceptibility in any other part of the body. In other words, the local trauma is the cause of the local development of malignancy. In many such cases the corporeal resistance may prevent any such newgrowth from implanting itself elsewhere in the body, until such time as corporeal cellular resistance is turned into cellular susceptibility. But more of this later.

I am decidedly of the opinion that, though local malignancy may develop through local adjuvants, the other parts of the body may not only be not susceptible to invasion, but may be decidedly inimical to it. Such are the cases, which, when the malignancy is locally eradicated by whatsoever means, become permanent cures and, *per contra*, trauma may initiate a local newgrowth in a resistant tissue where other organic areas are more susceptible. In these cases the metastases may outgrow the primary focus. In this respect malignancy follows closely the rules that govern infection, except that the mortality following malignant invasion is higher, owing to the lack of progressive immunity such as is obtained under infections. Herein lies the great difference between diffuse malignant invasion, and acute and chronic infections. In malignancy the chief trend seems to be towards a loss of any natural immunity, whereas in infections the toxaemia, in most cases, seems to heighten defence.

A Study of Metastasizing

Metastases from a malignant growth may reach remote areas by two distinct routes: (1) by the lymphatic chain, and (2) by the blood-stream, or (3) by a combination of both. There is nothing new in that, of course. But we must ask ourselves, do all the cells which detach themselves from the primary growth survive in their new environment? Or, if not, do they all perish? Or, if not, can they lie dormant for years in uncongenial surroundings to light into activity when more favourable circumstances develop? And, if so, have we any knowledge of the length of time such dormant potentiality may continue? As pointed out above, local susceptibility due to trauma may develop when clinical evidence as gathered from the course of the disease points to a general corporeal immunity. In such circumstances the local invasion may remain local for an indefinite period and local eradication then usually portends a cure. On the other hand, local and corporeal susceptibilities may be found in various degrees and, therefore, the local

manifestation may vary in all degrees of extension in comparison with the metastatic growths. In many instances the remote metastases may so dominate the clinical picture that the primary invasion remains insignificant and may be completely overlooked. The same conditions obtain in infections, to the degree that the parallel is almost, but not quite, perfect.

As regards the development of metastases, can we form any conception of their *modus operandi*? From a study of clinical cases of malignancy, several hypotheses immediately present themselves for consideration.

Do malignant cells from a newgrowth escape in showers into the circulation? Is it a matter of indifference whether it be direct into the blood-stream or through the intermediary lymphatic chain? Or does only an occasional malignant cell detach itself and invade the system? Here again a parallel is found in blood-stream infections.

But as regards malignancy the much more important question follows naturally upon the above: what happens to these blood-stream invasions? Do they survive for years in the blood-stream, or is the circulation freed from them? If the blood-stream is soon cleared of these cells, what happens to them? Are they digested in the blood-stream or do they become localized? And if localized in the tissues, are they destroyed immediately or may they remain in a state of suspended animation, to revive in more favourable circumstances? Let us see what clinical evidence we can bring to bear upon these questions.

Let us study a few enlightening cases.

1. A case of chorionepithelioma. We know that chorionepithelioma is a malignancy of syncitial and Langhan's cells. We know also that throughout the stages of normal placental development these cells invade the maternal blood-stream in large numbers, causing emboli in liver, spleen, brain, and so on. Yet eventually they are all liquidated by the enzymotic action of the body liquids. Occasionally however, under the stimulus of an abnormal endocrine agency, they get the upper hand and the most malignant type of newgrowth develops. Some years ago, I confined a primipara. Judging in retrospect, everything about her labour and recovery was as normal as could be. Eight months later she went to her physician complaining of severe pains in her bones. This had come on suddenly within the past 2 weeks. X-rays showed her vertebrae and long bones riddled with newgrowth. The lungs were widely invaded also, and metastatic newgrowth of the chorionepitheliomatous type was suspected. Examination revealed a normal pelvis with a normal involuted uterus. Menstruation since delivery had been regular and normal. She died after a short illness and the diagnosis of chorionepithelioma was confirmed. Gross and microscopic examination of the uterine wall showed not a trace of newgrowth there, nor any other distinguishable primary growth from which these metastases had proceeded.

Were some, or even one, of the usual normal placental blood invasions not destroyed during those intervening 8 months? If we concede this, they must have remained in a dormant potential state during a great part of that period, only to break down the natural body immunity by their excretions, finally to establish a comparative symbiosis and an eventual ascendancy. There comes considerable elucidation of this difficult and occult subject from two different types of cases of fairly recent date. In my monograph on "Endometriosis" (now in the press) are details of 2 cases of stromatous endometriosis with malignant properties. Both these cases

were followed over a period of 10 and 12 years respectively. Endometriosis is a disease that is restricted to the organs which lie in the pelvic region. The exceptions to the rule are so few as to be curiosities. I laid emphasis upon the fact that the susceptibility of the pelvic tissues is due to their propinquity to the source of the ovarian secretions. The nearer the structures to this source, the greater their susceptibility to implantations of endometrial ectopic cells. We have in this a very pronounced selectivity of endometrial cells for a certain specific, chemically impregnated tissue. I have maintained for years that selectivity, be it either bacterial or cellular, is the basis of disease specificity. The underlying cause of this selectivity or susceptibility is undoubtedly biochemical, be it endocrinological or metabolic, whether these be hereditary or acquired.

In these 2 malignant endometriotic cases, though the ovaries had been removed upon discovery of the disease, and though each had had repeated series of deep X-rays, nevertheless the spread of the disease in the pelvic structures continued with remissions over a period of 10 and 12 years. The long periods of remissions were due to the stunting effect of ovarian ablation and to the stunning effect of the X-ray treatments. In spite of these two factors which are usually curative these cells not only were able to survive the ablation of the ovaries, but became so inured to X-rays that they became X-ray fast.

Roentgengrams of the whole body of one of these cases immediately following death were negative, and gross examination at autopsy did not show any evidence of metastases outside the pelvic region, yet the microscopic studies of the lungs revealed legions of small metastases throughout the lungs. The second case, upon which I could not secure an autopsy, was X-rayed one month before death and the lungs did not show anything abnormal, yet another picture taken just before death revealed the lungs in a state of 'snow-storm' from thousands of metastatic growths resembling a miliary tuberculosis. It would seem that certain clear inferences may be drawn from these cases. The susceptibility of the pelvic tissues and the non-susceptibility of the extrapelvic areas to the newgrowth was maintained throughout 10 and 12 years, until such time (death was due to uremia from ureteral obstruction in both cases) as the tissue individualistic characters were submerged in the poisons which flooded the system, making the extrapelvic tissues susceptible just before death. It also tends to confirm the opinion that the malignant cells may increase in hardihood owing to any prolonged resistance that they may have to overcome, and that as body resistance, which means tissue specialization, is lost all are subdued to the malignant invader.

But there is a deeper lesson to be learned from these 2 cases. I doubt if anyone could maintain that malignant cells got free in the circulation only when the extrapelvic susceptibility was established, and that in that last month of life the body was flooded with millions of dispersed cells. Rather must one infer that throughout these 10 and 12 years malignant cells invaded the blood-stream just as do bacteria in pyaemia, but that, owing to the uncongenial surroundings, they were overcome and destroyed, and that the survival of the malignant cells of this continued blood-stream invasion was possible only when biological tissue differentiation was lost in the last months of life. In these cases, as distinguished from the case of chorionepithelioma cited above, there was always a primary source in the pelvis to supply the seeds. In the case of chorionepithelioma such a primary source could not be found in the uterus. The inference here must be that

there must have been a potential dormant nidus (dormant for 8 months after delivery) somewhere in the body, not necessarily in the uterus, though this be the common site of such chorionic activity.

Another recent case is of special interest, A patient, 37 years of age, had a radical breast operation for a small malignant tumour. This was immediately followed by a series of deep X-ray treatments. Fifteen months later she complained of flashes of light in one eye. Wasserman and tuberculin tests proved negative. Roentgengrams of the whole body were negative at that time. Three months later the other eye became similarly involved and total blindness followed. X-ray examination of the bones of the body again proved negative. Six months later she complained of severe pain in the back. X-ray examination now revealed a metastatic involvement of two vertebrae and two ribs. The symptoms have grown progressively worse, due to continued anorexia, nausea and gradually increasing cachexia.

Here is a case in which selectivity of cells has reached a high degree. The inference, I think, is here again justified that malignant cells which reach the circulation are for a long time destroyed, but that eventually, by their destruction, a progressive symbiotic chemical balance is established first in one tissue, then in another, eventuating in a generalized corporeal susceptibility. I think the contention cannot be maintained, as is frequently held, that all aberrent malignant cells are destructive. On the contrary, their power to localize and flourish is dependent upon corporeal and organic resistance which, however, usually gives way slowly under the repeated and increasing invasions. Special organs, or parts of organs will differ in the time and the degree of their tolerance of the invasion, which will explain how one special tissue, such as two choroids in my case, became the first organs to yield to the flood.

Comparing the size and singleness of the optic artery with the blood-vessels of the rest of the body, it is estimated that a single malignant cell which had escaped and reached the circulation would have to complete the round of the circulation from 1 to 10,000 times before chance landed it in a single choroid, and this chance of a single cell would have to be repeated before the other choroid was attained. In this case 3 months elapsed. This case is a striking example of specificity of newgrowth cells for certain definite, restricted areas of favourable biochemical composition. We are forced to the conclusion that invasions of the blood-stream are frequent and progressively copious, but that few of these survive the freedom of the circulation or the stasis of inimical organs. Any susceptible tissue, though the first to be involved with metastases, may be surpassed and overshadowed later by the rapidity of other metastatic growths. It is quite evident that different tissues may lose their immunity quickly to newgrowth, but to a lesser degree than other tissues that have resisted longer, but the defence of which, when once overcome, collapses to a more profound degree. That is evidenced in these quoted cases by the longer resistance of the bones, but finally, when their resistance was broken, the newgrowth flourished like the proverbial bay tree. So the stages of metastasizing would seem to be destruction, inimical tolerance, pacific symbiosis, and lastly, surrender to the uninvited guest.

The concept that floods of malignant cells are constantly invading the blood-stream, and localize and thrive only where the soil is favourable, carries with it the explanation for the frequent bilaterality of metastases in similar bilateral organs. For example, the constant bilateral invasion of the ovaries in Krukenberg's tumours;

the involvement of both ovaries in malignant papillary growths; the frequent involvement of both breasts in malignancy; the involvement of many vertebrae before other bones are involved in metastases from breast malignancy; the contamination of the choroids of both eyes before any other parts of the body were affected, in the case cited above.

But aside from the corporeal resistance of special organs there are factors inherent in the malignant cells themselves which determine to a certain degree the frequency and numbers of cells set free in the circulation. There are two commonly known characters and doubtless many other less understood. These are: (1) the size of the malignant cells; and (2) the character of the supporting tissue about the malignancy.

In these respects malignancy resembles infections. The larger organisms of infection, such as syphilis, for example, take a long time before reaching the general circulation, and if the primary focus of infection can be eradicated, the septicaemic stage may be avoided. The spirochaete is at one extremity of size differentiation. At the other extremity are the ultramicroscopic organisms of virus diseases which reach the circulation almost directly.

The more rapidly a malignant cell multiplies the smaller and more embryonic will be its progeny and, therefore, the quicker it will invade the lymphatic and blood-stream.

On the other hand, the degree of succulence and vascularity of the matrix primarily invaded will determine the facility with which malignant cells may escape into the lymph or blood-streams.

All these are chiefly mechanical factors quite apart from the biochemical adjuvants and inhibitors, inherent or developed in the liquid and semi-solid tissues of the body.

Malignancy is commonly a tissue disease, that is, its growth and its metastases settle in semi-fluid tissues, but leucaemia, which is a malignancy of free cells, finds its habitat in its normal site—the blood.

Conclusions

Malignancy, to the clinician and pathologist, is a relative term. In the vast majority of malignant cases aberrant malignant cells are constantly invading the blood-stream. These are usually rendered impotent for various periods by the body fluids, or cells. The common concept that malignant cells are not destroyed, but remain long in the circulation, is not sustained by a careful study of clinical cases. Local territorial cancer is usually primarily met by a resistance outside that territoriality. This extra-territorial immunity or lack of it, determines the slowness or rapidity of the metastasizing process.

Tissues differ in the time and the degree of yielding their immunity to the invading cells. Under the influence of repeated invasions a tolerance between the host's tissues and the uninvited guest is eventually established to the ultimate destruction of the patient. Frequent blood invasions and the similarity in biochemistry of bilateral organs and the predilection of certain types of malignant cells for that environment determines the simultaneous bilateral incidence of metastases in those organs.

Lord Rutherford stated that atoms behaved as if they were endowed with intelligence. I have repeatedly asserted that the selectivity of microbes for certain tissues is the specific property which gives diseases their diagnostic characters. Cancer cells possess this selectivity to a higher degree than microbes, and it determines their clinical courses.

A Case of Obstructed Labour due to Dysgerminoma

BY

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THE patient, Mrs. S., a primipara aged 22 years, was transferred from the Radcliffe Infirmary Maternity Home to my ward on March 9th, 1937, as a case of obstructed labour.

She had been attended by a midwife in the country and had been, I believe, in labour for 48 hours before she was seen by a doctor, who immediately sent her into hospital.

History of pregnancy.

There was no abnormality and labour began at the expected time.

On admission to the Maternity Department she was found to be much exhausted, the head was above the brim and the os undilated. The foetal heart could not be heard. A firm mass could be felt in the pelvis which appeared to be preventing the descent of the head. After treatment and rest her condition improved and as no advance was made in spite of good pains I was asked to see her, with a view to Caesarean section.

On examination.

The patient was a small but well-developed woman, tired and worn out. The uterus was contracting well but the head could not be pushed into the pelvic inlet and there was marked over-riding. The foetal heart could not be heard.

I found a very curious tumour in the pelvis; it lay behind the lower segment of the uterus and felt like the lower segment of a large bun, jammed between the head and the sacrum. Its surface was almost smooth and it was firm and solid—not cystic—in consistence. It appeared to be about 5 inches in diameter and much flattened from before backwards. It was presumably an ovarian tumour but of a type with which I was unfamiliar.

Operation. As the condition of the patient had now improved I opened the abdomen and removed a dead male child through a low vertical uterine incision which I covered with the bladder reflection of the peritoneum.

The tumour was seen to have the size and shape ascribed to it and to be a growth of the right ovary but as the patient's condition was none too good an attempt was not made to remove it and the abdomen was closed.

Convalescence was complicated by a streptococcal urinary infection which, however, soon yielded to treatment.

On July 1st, 1937, the patient reported that she was suffering from menorrhagia, but was otherwise in good health.

On July 13th, 1937 I operated again and found the tumour rather larger than before and adherent to the structures in its neighbourhood. The adhesions were separated without difficulty and the tumour removed. As it did not appear to be a malignant growth I did not perform a panhysterectomy. The patient made an uneventful convalescence and was discharged on August 7th, 1937.

I saw the patient last on March 21st, 1942. She is in excellent health. Her weight is satisfactory, she looks well and she has

no complaints except, recently, occasional menorrhagia.

On examination there is no pelvic, abdominal or other abnormality.

For the pathological report and review of the literature of these rare tumours I am indebted to Dr. Robb Smith, Director of Pathology, the Radcliffe Infirmary, Oxford.

Pathology.

The specimen consisted of a whitish oval tumour weighing, when fixed, 910 grm. and measuring 14.5 × 12 × 8 cm. The surface was irregularly lobulated; at one point the Fallopian tube could be recognized and appeared natural. The cut surface was of a uniform cream colour in which ran bands of translucent material, and at the centre there appeared to be some liquefaction. It was everywhere encapsulated.

Histology. (R.I.S.H. 63193.)

The tumour consists of collections of large round cells arranged in columns or masses lying in a fibrocellular stroma.

The tumour cell is oval, measuring (in paraffin section) 15 × 12 with a nucleus 12 × 10. The cell membrane is indistinct and the cytoplasm is faintly eosinophil and finely granular. The nucleus is round to oval with a dense nuclear membrane. There is a solitary prominent nucleolus. The nucleus is rich in basic chromata which is arranged in the form of nodes with fine threads joining them. The nucleoplasm is colourless. Binucleate forms are frequent and numerous cells show karyokinesis.

The supporting stroma divides the collections of cells into columns or islands. This stroma is profuse and consists of collagen and reticulin fibrils in which are lying fibrocytes and reticulum cells. A striking feature is the large number of small lymphocytes and histiocytes in the stroma, and many of the latter have formed giant cells. This cellularity of the stroma is most marked in the region of the blood vessels and in some places the histiocytic giant cells and lymphocytes recall a 'tubercle' though there is no necrosis or caseation. There are no strands of reticulin between the tumour masses. The tumour is not highly vascular and there are numerous areas of degeneration probably due to this fact. There is very little fat in the tumour and it chiefly occurs in the histiocytic giant cells. Normal ovarian tissues could not be made out.

Histogenesis.

This type of tumour occurs in both sexes, though there are striking differences in age incidence (in females in the second and third decades; in males after the fourth decade) and in prognosis (in females it is almost invariably benign, in males highly malignant, though Payne[1] has shown that the prognosis is better than is generally thought). Its relation to the gonadal tissue was first recognized in those occurring in males and Chevassu[2] suggested that they should be called 'seminome.' Similar tumours were frequently found in cryptorchids and Peyron[3] described the ovarian form of tumour, suggesting that they were derived from the medullary cords which had differentiated towards male elements.

However, the matter was classified by Meyer[4] who proposed the name dysgerminoma and suggested that they were derived from cells of the germinal epithelium which have not been determined to cells of either male or female type. This is in keeping with the observations that they frequently occur in hermaphrodites or persons with poorly developed genitalia and that they do not show any evidence of hormonal activity.

The general view is that these tumours in the female are essentially benign though

Wolfe and Kaminester,[5] and Doubriere[6] have described cases with definite evidence of malignancy and the former authors regard the prognosis as poor.

Portions of the specimen are preserved in the museums at the Radcliffe Infirmary, Oxford, and St. Bartholomew's Hospital, London.

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DYSGERMINOMA.

Fig. 1. The surface of the tumour (natural size).

Fig. 2. The cut surface of the tumour.

Fig. 3. Showing the general structure of the tumour. × 100.

Fig. 4. Showing histiocytic giant cell. × 210.

Fig. 5. Showing the character of the tumour cells. × 440.

FIG. 1.

FIG. 2.

FIG. 3.

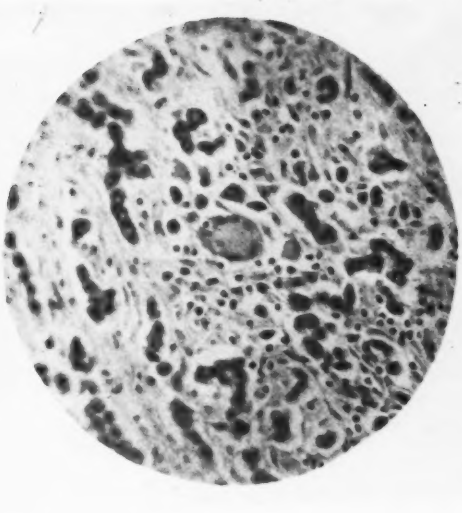

FIG. 4.

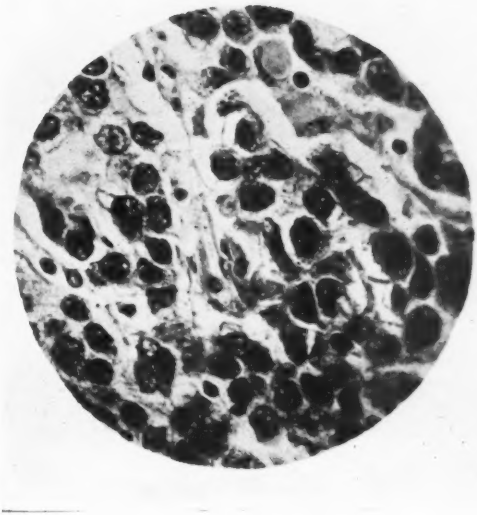

FIG. 5.

A Case of Full-time Hydatidiform Mole with Central Placenta Praevia

BY

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THE following case of hydatidiform mole shows some interesting features.

CASE HISTORY.

Mrs. O'D., an Irishwoman, aged 32 years, was admitted as an emergency case of antepartum haemorrhage to the maternity wards, Dundee Royal Infirmary, on June 21st, 1941. She had had 2 normal confinements in 1932 and 1939 respectively, and a 2 months' miscarriage in July, 1940. Her menstrual periods had always been regular, the last one being on September 26th, 1940. She had not booked with her doctor until late on in her pregnancy, but her blood-pressure and urine were normal at each visit thereafter and her general health was good. Breast enlargement took place as usual, and supposed foetal movements were felt right up to the day of admission, though less than with previous pregnancies. Growth of the abdomen was progressive throughout the pregnancy though the patient thought her abdomen was unusually large. There was not any bleeding or discharge until the fortnight before admission, when a brown discharge was present intermittently; neither was there any visual or urinary disturbance. Oedema of the feet appeared during the last 2 weeks and increased in the 4 days before admission.

On rising from bed on the morning of June 21st there was a sudden painless flood of blood on the floor. The patient went back to bed and the bleeding stopped. The doctor was summoned, and on his arrival there was further bleeding. Backache was now being felt. A vaginal examination revealed a boggy mass over the internal os, which was one finger dilated. The patient was sent into hospital with a diagnosis of placenta praevia.

On admission she was seen to be a well-nourished woman with fairly good colour but rather a toxic appearance. Gross oedema was present in the lower limbs and slight oedema in the lower part of the abdominal wall. There was not any noticeable oedema in hands or face. The blood-pressure was 180/120 and the urine contained albumin. The temperature was 97.4°F., pulse-rate 88, and respiration-rate 20. She complained of backache but not of abdominal pain. There was not any fresh haemorrhage, though traces of previous bleeding were seen about the vulva. The abdomen was the size of an exceptionally large full-time pregnancy, and had the firm feeling associated with a partially-concealed accidental haemorrhage. Foetal heart sounds were not heard and foetal parts could not be palpated. A diagnosis of probable accidental haemorrhage was made. She was given an injection of $\frac{1}{4}$ grain morphine sulphate and slept for an hour. The pulse-rate was watched, and remained steady at 88 per minute. When she woke up she complained again of backache, but there was not any further bleed-

ing. Two hours after admission a vaginal examination was made without an anaesthetic. The cervical os was found to admit one finger but the cervix was hard and did not suggest that the patient was in labour. Placental tissue was felt covering the internal os. Bleeding did not occur during this examination, though some old blood was present in the vagina. Even with fundal pressure, by an assistant, foetal parts could not be felt through the placenta, and a diagnosis as to the presentation could not be made. In view of the central placenta praevia preparations were made for immediate Caesarean section.

Operation.

The patient was anaesthetized with general ethyl chloride and ether. Even under the anaesthetic foetal parts could not be palpated. The abdomen was opened through a right paramedian incision extending above and below the umbilicus. The tissues appeared to be rather bloodless, so that bleeding in the abdominal wound was minimal. The uterus was normal in colour and appearance though unduly large. The abdominal cavity was packed off and the classical operation was performed. An enormous vesicular mole was found to be filling the uterine cavity. It was removed in handfuls, vesicles and fluid being ladled out into buckets on the floor. The mole came away very easily, and appeared to have only slender attachments to the uterine wall. There was scarcely any bleeding during the removal of the mole, and the uterus contracted well. The placenta was found to be covering the lower uterine segment as a complete central placenta praevia, and was stripped off by hand. It was more firmly attached than normally to the uterine wall, and some bleeding occurred during its separation. The uterus then contracted down and appeared to be empty apart from some blood and detached vesicles. There was not any sign of infiltration of the uterine wall by the mole, and the organ looked healthy inside and out. Hysterectomy, therefore, did not appear to be indicated. Pituitrin was injected into the uterine wall to maintain contraction and retraction and the incision was sutured. In spite of the abdominal packs vesicles had been spilled into the peritoneal cavity; these were removed so far as possible, though some inevitably must have been left behind. Unfortunately note was not made of the state of the ovaries, though had any gross enlargement or cystic condition been present it would almost certainly have been noticed during the clearing up of the pouch of Douglas. The abdomen was closed. The patient's general condition at the end of the operation was satisfactory. Her pulse was of good quality and the rate 104 per minute, and the uterus was well contracted. Some vesicles and blood were found to have been passed *per vaginam* during the operation.

Specimen.

The hydatidiform mole was composed of vesicles varying in size from tiny ones to those the size of large raisins. Much fluid had also been evacuated from the uterus as though the vesicles were bathed in it. There was not any sign of a foetus or umbilical cord or amniotic sac. The placenta had a normal surface area for a full-time pregnancy but was a good deal thinner than usual, was not divided into cotyledons, and merged indefinitely at the edges into ill-defined membranous tissue from which the vesicles arose. It looked as if the chorionic space had been obliterated, and the vesicles appeared to be attached to the upper or foetal surface of the placenta. Blood-vessels were not

present on the surface of the placenta. Microscopical examination of a piece of placental tissue showed it to have a rather dense, fibrous structure. The villi showed hydatidiform degeneration with absence of vessels, but there was little or no proliferation of the trophoblastic epithelium on their surface.

Puerperium.

On the day after operation the temperature rose to 105.4°F., and the pulse-rate to 130. The patient was extremely hot and dry and slightly delirious. The blood-pressure was 120/65 and the urine did not contain any pus cells. The abdomen was soft, but a few scattered rhonchi were present in the chest. The pyrexia did not appear to be associated with sepsis but rather to be of the nature of a heat-stroke, the day being exceptionally hot. Another possibility was that the hyper-pyrexia was of an anaphylactic nature resulting from absorption of toxic fluid by the opened-up uterine sinuses during the operation, or even, perhaps, from the presence of the stray vesicles in the peritoneal cavity. The treatment given was ice-bags to the head, Dover's powder, and sulphonamide as a precaution. The next day the patient was better, the temperature falling to 103.4°F. and the pulse-rate to 110. She was taking fluids well, was passing urine normally and did not have any complaints. The blood-pressure was 110/62, and the urine contained only a trace of albumin. The temperature fell by lysis, reaching 98.8°F. on the 4th day. There was another sharp rise to 103°F. on the fifth evening without any symptoms, falling to normal in 24 hours and remaining normal for the remainder of her stay in hospital.

Engorgement of the breasts was appearing by the 3rd day with consequent discomfort; a course of stilboestrol tablets was, therefore, given over a few days and successfully inhibited lactation. The lochia were normal apart from containing vesicles for 24 hours after the operation. By the 6th day, as she was looking rather pale and her haemoglobin was only 50 per cent, a blood examination was made and excluded any serious blood disease. A transfusion of 1 pint of citrated blood was given on the 7th day, with general improvement. Thereafter 30 grains of ferr. et ammon. cit. was given 3 times daily. The abdominal incision healed normally. Albuminuria disappeared after the 7th day, and the blood-pressure remained steady at about 130/80. She was allowed up on the 16th day and discharged home in good health on the 21st day.

Specimens of urine submitted to the Pregnancy Diagnosis Laboratory, Edinburgh, for Aschheim-Zondek tests were taken 48 hours and 21 days after operation. The reports read: "Positive, rather a weak reaction," and "Negative" respectively. The Wassermann reaction was also negative.

Subsequent History.

The patient reported on October 13th, 1941, in good health. The Aschheim-Zondek test was negative. She had had a period lasting 6 days exactly 6 weeks after the operation, followed by another two periods lasting 4 days each at regular monthly intervals. Pelvic examination showed the uterus to be completely involuted and lying anteriorly, the vaginal walls and cervix were normal and there was not any discharge. The abdomen was flat and did not show any abnormality. The blood-pressure was 134/80 and the urine clear of albumin. The haemoglobin was 106 per cent. The patient's only complaint was that her hair was falling out badly.

She reported again on April 4th, 1942, when the Aschheim-Zondek test was again negative; she was still well and her hair had grown in again. The patient, who now weighed over 12 stone, had put on 7 pounds since the operation. Menstrual periods were regular and normal each month. The blood-pressure and urine were normal. On June 25th she again reported well, and on August 6th the Aschheim-Zondek test was still negative.

Discussion.

It is generally agreed that the true hydatidiform mole as we know it clinically, without placenta or foetus, or at most with an imperfectly developed foetus, is the result of hydatidiform degeneration of the entire chorion in the early weeks of pregnancy before the placenta has had time to form. The mole continues to grow and is usually expelled some time in the first half of pregnancy. De Lee[1] states that the entire chorion is usually involved, but that either the chorion frondosum or chorion laeve may be alone affected. The ovum, he says, is primarily diseased. In the case I have recorded it would appear that the hydatidiform change affected the entire chorion and occurred not in the very early weeks but as the placenta was developing. The foetus presumably perished. Cases have been recorded in which a partial hydatidiform degeneration of the placenta has been recognized later in pregnancy, even with the birth of a live, normally-formed child. My case, in point of time of onset of the vesicular change in relation to the period of gestation, would appear to fit in between these two extremes.

Hertig and Edmonds,[2] in a series of 1027 spontaneously aborted ova, found that early hydatidiform changes could be shown microscopically in the villi of 40 per cent. In about half of the whole series the ovum was "pathologic," i.e. defective or absent, and in the other half "non-pathologic" or normal. Hydatidiform degeneration however occurred about 6 times as frequently in the "pathologic" as in the "non-pathologic" group. The authors explained these changes in the villi, which they considered physiological rather than pathological, as follows. The foetal circulation should start functioning at about the 5th week of pregnancy. If the foetus is absent or defective the circulation cannot function. But the chorionic epithelium in contact with the maternal sinuses continues its normal activity, and fluid accumulates in the villi by absorption and/or secretion, as there is not a foetal circulation to carry it away. These investigators, like others, found that the classical hydatidiform mole is uncommon, and either is not associated with an embryo at all or rarely with a very defective one. They consider that the classical mole is derived from the earlier type described, which for some reason fails to abort at the usual time.

It must be very unusual to find a placenta associated with a hydatidiform mole, and even more extraordinary to find the placenta as a central placenta praevia. Why the placenta should have continued to grow long after the foetus presumably perished is difficult to understand, as it did not serve any physiological purpose. Its continued growth can only be considered pathological, as indeed the microscopical appearance of its structure confirms. Presumably the hydatidiform villi in the placenta went on expanding just as the rest of the mole grew, and the fibrous tissue formation suggests a defensive reaction on the part of the maternal organism.

I cannot find any record of a full-time hydatidiform mole in the literature, though references are made to cases which went to term or even over. De Lee saw only one case of vesicular mole which did not ter-

minate before the 6th month, and in that one the mole ceased growing and was expelled at term. He refers to cases of Depaul and Madden which went over term. Brews[3] mentions 2 cases with amenorrhoea of over 40 weeks, and refers to a case of Blair-Bell's in which amenorrhoea of 10 months was associated with a carneous hydatidiform mole which enlarged the uterus to the size of a 12 weeks' pregnancy only. Brews, incidentally, points out that cases recorded in the literature of vesicular moles with an abnormally low or negative hormone assay are probably cases of "missed" abortion of the separated mole. This raises the question in one's mind whether some of the cases referred to in the literature as going to term, or over, were really just cases of "missed" vesicular molar abortion.

The absence of any antenatal hormone investigation in my case makes it difficult to say whether it was a case of "missed" abortion or not, but the enormous size of the mole, the steady increase in enlargement of the abdomen as noticed by the patient and the presence of a weakly positive Aschheim-Zondek test 48 hours after the evacuation of the uterus all suggest that the mole was still growing up to the time of its removal. The blood-stained discharge which occurred during the fortnight preceding admission to hospital, and the bleeding on the morning of admission, were obviously the result of a slight separation of part of the low-lying placenta.

Cases of hydatidiform degeneration of the placenta associated with a normal foetus have been observed by various writers. Ganner[4] and Barnes[5] have each published a case in which the condition was present with a central placenta praevia.

Toxaemia is often associated with a vesicular mole. Sherman[6] found it to be present in 29.4 per cent of a series of 78 cases, and this seems to be about the usual figure. In my case toxaemia was so well marked that it at once suggested a diagnosis of accidental haemorrhage rather than the correct diagnosis of placenta praevia which the patient's doctor had made by vaginal examination. The patient stated that she had felt foetal movements throughout the pregnancy. In view of the enormous bulk of the mole and associated fluid it might almost have been surprising if she had not felt movement of some sort inside her. An even more interesting phenomenon was Nature's effort to produce a milk supply for a foetus which presumably perished early in pregnancy.

At the operation there was not any penetration of the mole into the uterine wall. The Aschheim-Zondek reaction, which was only weakly positive 48 hours after evacuation of the uterus, did not suggest that the mole had been of an actively proliferating kind. One can only conjecture as to the fate of the stray vesicles left inside the abdomen, but probably they would soon perish. The subsequent negative Aschheim-Zondek tests up to 13 months after operation were very satisfactory, and suggest that chorionepithelioma will not develop.

It is generally agreed that, following hydatidiform mole, a period of time may elapse when the Aschheim-Zondek test is negative, even though chorionepithelioma may ultimately develop with a return of the positive reaction. Payne,[7] in a study of the relevant literature, finds that the longest latent period recorded between the antecedent pregnancy and the development of chorionepithelioma, prolan tests being taken frequently and showing negative results, is 6 months. This author considers that after the first negative test following expulsion of a mole a follow-up of at least a year is necessary before the possibility of malignant degeneration can be ruled out. Mathieu[8] on the other hand gives as his opinion that the Aschheim-Zondek test

cannot be negative in the presence of living chorionic tissue and that, following hydatidiform mole, the finding of 2 or 3 negative tests (sufficient to avoid the possibility of a laboratory error) means that chorionepithelioma will not develop.

That normal pregnancies may follow vesicular mole is generally understood. There does not appear to be general agreement, however, as to whether there is a tendency to recurrence of the condition in subsequent pregnancies.

Summary.

1. A case of full-time hydatidiform mole without a foetus but with a central placenta praevia, and associated with severe toxaemia, is described.

2. The treatment by Caesarean section in view of the central placenta praevia revealed the true condition.

3. Interesting points about the puerperium such as hyper-pyrexia and the appearance of breast secretion are noted.

4. A follow-up of 13 months showed persistently negative Aschheim-Zondek tests and a return to normal menstrual periodicity and good health.

5. The absence of a similar case in the literature is noted.

6. Points relevant to the case are discussed with reference to the literature on the subject.

I am indebted to Professor Margaret Fairlie for permission to publish this case, to Professor D. F. Cappell for the report on the specimen, and to both for helpful criticism and advice in the preparation of this paper.

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The Response of Isolated Muscle Strips from the Upper and Lower Segments of the Human Full-time Pregnant Uterus to Pitressin and to Pitocin *

BY

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THOUGH the vasopressor and the uterus-stimulating (oxytocic) activities of the posterior lobe of the pituitary have long been known, the chemistry of the active principle or principles responsible for these actions, has remained unsolved. There is even doubt as to whether the posterior lobe contains one or more hormones. Abel[1] and his fellow-workers supported the view that there is only one: Dudley[2] was of the opinion that there are probably at least three active substances present. Following, however, the publication,[3] from the research laboratories of Parke, Davis and Company, that the vassopressor and oxytocic principles had been separated almost completely, the presence of at least two hormones was generally accepted. These two principles, marketed under the trade names "pitressin" and "pitocin," have since been widely used in clinical practice; the former chiefly as an intestinal stimulant and anti-diuretic; the latter as a uterine stimulant especially in cases of pregnancy toxaemia for which the absence of pressor and anti-diuretic properties is clearly an advantage.

OXYTOCIC AND PRESSOR STANDARDS.

Pitocin, like the liquid extracts of the posterior pituitary included in both the British Pharmacopoeia and the United States Pharmacopoeia, is standardized by comparing its oxytocic activity on the exsected uterus of a virgin guinea pig, with that of a solution of international standard powdered pituitary; the residual oxytocic activity of pitressin is estimated by the same biological test. The virgin guinea pig is used for this oxytocic assay, a fact that must be emphasized, because in this paper it will be shown that the reaction of the exsected human full-time pregnant uterus to pitocin and to pitressin is very different from that of the exsected uterus of a virgin guinea pig.

Based on changes observed in the blood-pressure of anaesthetized dogs, a pressor standard[4] was introduced from the laboratories of Parke, Davis and Company, where it was proposed that 1 mg. of the United States Pharmacopoeia standard powdered pituitary should be considered as containing two pressor units. Though widely accepted in practice, this pressor standard has not been included in either the British or the United States Pharmacopoeias.

During the course of an investigation to study the effect of certain drugs on isolated muscle strips from the human uterus, it was

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found that pitressin was a powerful stimulant, an observation that has previously been made by other workers on strips from the early pregnant (Robson[5]) and the full-time pregnant human uterus (Adair and Haugen[6]). Moir,[7, 8] Adair and Davis,[9] Gardiner and Bradbury[10] and McLellan[11] have made similar observations on the non-pregnant, early pregnant, and full-time pregnant human uterus *in situ*.

This paper is a preliminary report on a quantitative comparison between the effect of pitressin and that of pitocin on isolated muscle strips from the full-time pregnant human uterus. A striking difference between the reactivity to posterior pituitary extracts of the upper and the lower uterine segments will also be described.

Material.

All the muscle strips used for this investigation were removed from the uterus at Caesarean sections performed either by myself or in my presence. Special note was made of the exact part of the uterus from which the strip was taken and the direction of the muscle fibres.

The commercial preparations of pituitary used were "pitressin" and "pitocin" (Parke, Davis and Company) obtained from the hospital dispensary. A quantity of more highly purified pitressin (Rx 097376) and pitocin (CE1857), prepared for research purposes and kindly supplied by the manufacturers, was also available; throughout this paper the purified preparations have been used unless otherwise stated. Each c.c. of "purified" pitocin contained 10 oxytocic units* and 0.4 pressor units: each c.c. of "purified" pitressin contained 10 pressor units and one oxytocic unit.

* One oxytocic unit of posterior pituitary is the same as one international unit which is equivalent to 0.5 mg. of international standard powdered pituitary.

Method.

The tissues obtained were placed in cold Locke's solution and taken to the laboratory. Strips, half to one inch in length, were cut and suspended in oxygenated Locke's solution at a temperature of 37°F., the bath containing 50 c.c. Tracings were made by Gimball levers on smoked drums, contraction of the uterus being recorded by the upstroke of the lever. The time marker recorded intervals of 1 minute. All published tracings are reversed negatives; they should be read from left to right. The temperature in the outside bath was kept constant to ½°F. by an electric thermostat. Any tissue not immediately required was kept in the refrigerator (4°C.).

Even though the uterine muscle strip was placed in the bath within a few minutes of its removal at operation, several hours usually elapsed before it settled down into its new environment and was contracting steadily. Though the form of the tracing varied with such factors as the length of the strip used, the leverage employed, and the speed of the drum, any response that followed the use of a particular preparation was reasonably constant and did not appear to alter with the varying patterns which the tracing may previously have shown; this is in accord with the findings of other workers.[6] It was regarded as a motor response if the uterus showed either an increase in tone or an increase in the frequency or extent of the individual contractions. An increase in tone was the commonest motor defect observed.

In the Radcliffe Infirmary, the upper segment Caesarean section is rarely performed so the majority of the present experiments were made on muscle strips from the lower uterine segment. This statement requires amplification since all the strips were from patients not yet in labour, and there are some authorities who

do not consider that the lower uterine segment is differentiated until after the onset of labour. For the purposes of this paper, tissue from the lower uterine segment refers to that taken from the uterus well below the attachment of the loose peritoneum covering the front of the organ. Tissue from the upper uterine segment refers to muscle removed well above this level.

Reaction of the Lower Uterine Segment.

When a muscle strip from the lower uterine segment was tested by the addition to the bath (50 c.c.) of $\frac{1}{10}$th of a unit of pitocin or less, a definite motor response was not observed; with amounts greater than $\frac{1}{2}$ a unit there was a fairly constant slight motor effect. By comparison the result of 2 units of pitressin, added to the bath, was surprising; there was a strong motor response with a prolonged systolic effect, the base line rising to three or four times the height of the original contractions (Fig. 1). After changing the Locke's solution the experiment was repeated; it was found that $\frac{1}{20}$th of a unit of pitressin also provoked a powerful motor response, and $\frac{1}{100}$th of a unit a definite motor effect (Fig. 2). Further trials confirmed this observation. The evidence was clear: the pitressin was a more powerful stimulant than the pitocin when tested on muscle strips obtained from the lower segment of a full-time pregnant human uterus.

Response of the Upper Segment.

A study of the reaction of muscle strips from the upper uterine segment showed that, in contrast to the motor effects seen when the lower uterine segment was tested, the addition of comparable amounts of either pitocin or pitressin failed to produce any definite motor response. Large doses of both preparations had a slight motor effect. This difference in reactivity between the upper and lower uterine segments was thought to be of some importance; the

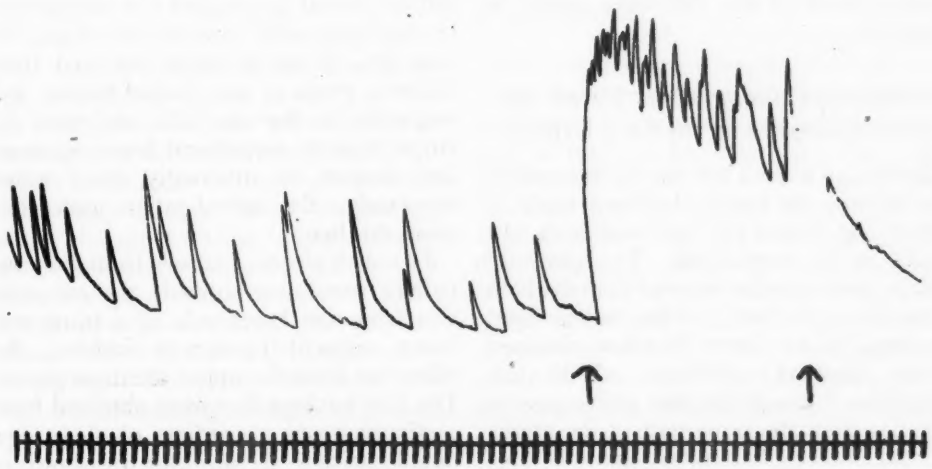

Fig. 1.

The response of the lower uterine segment to pitressin (human uterus).
1st arrow.....2 units of pitressin.
2nd arrow.....solution changed.

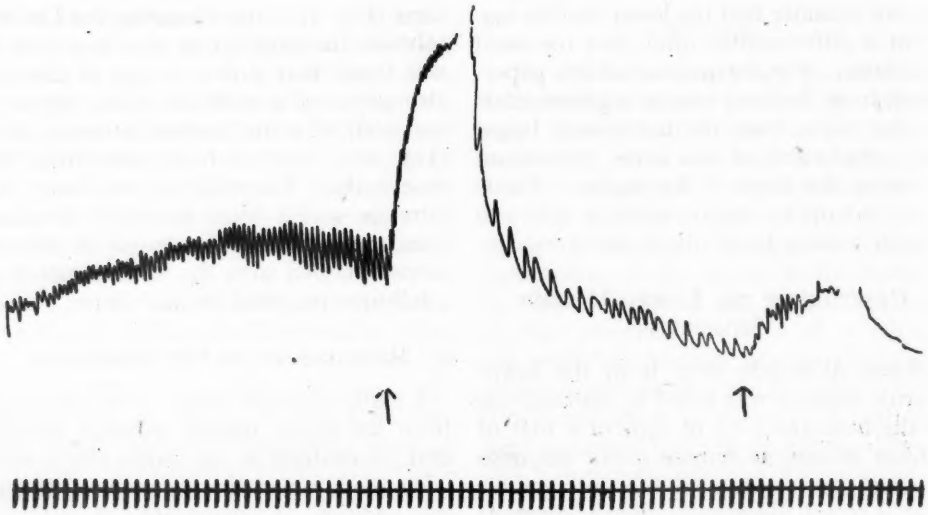

FIG. 2.

The response of the lower uterine segment to pitressin (human uterus)
1st arrow.....1/20th of a unit of pitressin.
Solution changed.
2nd arrow.....1/100th of a unit of pitressin.

technique was therefore changed so that clearer proof of this difference might be obtained.

COMPARISON BETWEEN THE UPPER AND LOWER SEGMENTS OF THE SAME UTERUS.

Instead of a small (50 c.c.) bath in which the experiments had so far been made, a larger one (100 c.c.) was used with two hooks on the central rod. Two pieces of uterus could now be suspended in the bath alongside each other, and two independent tracings, the one above the other, obtained under identical conditions. With this technique it was found that active muscle samples from the same part of the uterus reacted similarly to pituitary extracts, thus confirming a previous observation by Adair and Haugen.[6] No significant difference in reaction was observed between strips cut longitudinally and those cut transversely. As a search of the literature did not reveal any record of a comparison having been made between the actions and reactions of muscle strips obtained from different parts of the human uterus, and suspended in the one bath, and since the strips from the upper and lower segments had reacted so differently when tested separately, the investigation proceeded along this line.

Two such pieces of muscle from the same patient were now studied; the one strip was from the lower side of a transverse lower segment Caesarean incision, the other was from the upper uterine segment. The first tracings that were obtained from a simultaneous recording of these two muscle strips in the one bath are shown in Figure 3. The upper tracing corresponds to the upper uterine segment; the lower tracing corresponds to the lower uterine segment. The four arrows reading from

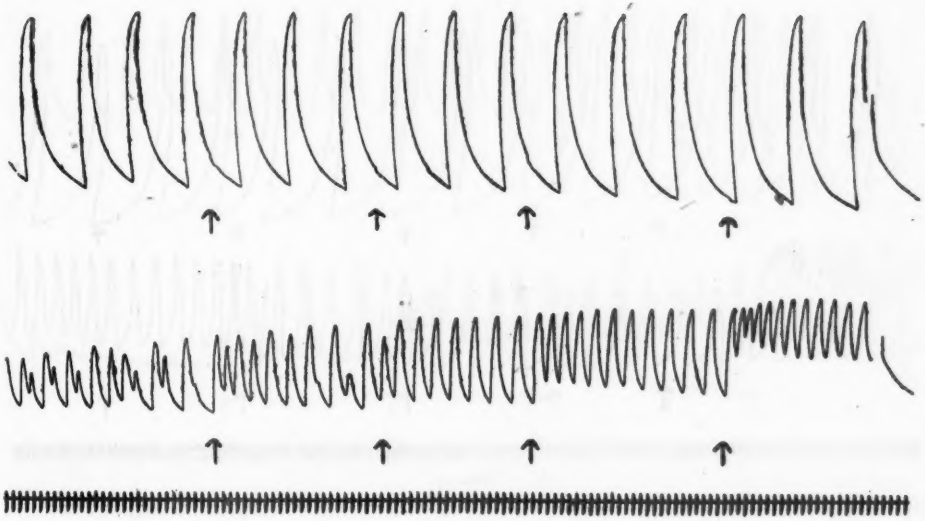

FIG. 3.

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the one uterus, showing the motor effect of pitressin on the lower segment, and the absence of effect on the upper segment (human uterus).

1st arrow.....1/100th of a unit of pitressin
2nd arrow.....1/50th of a unit of pitressin
3rd arrow.....1/10th of a unit of pitressin
4th arrow.....1/2 of a unit of pitressin

left to right represent the addition to the bath of $\frac{1}{100}$th of a unit, $\frac{1}{50}$th of a unit, $\frac{1}{10}$th of a unit and $\frac{1}{2}$ of a unit of pitressin. It will be seen that following each addition there is an increase in tone (motor effect) of the lower tracing (lower uterine segment). The upper tracing (upper segment) does not show any response, the pitressin having had apparently no effect. These tracings clearly confirmed the previous findings. After changing the Locke's solution the same two pieces of muscle were tested with increasing amounts of pitocin. Figure 4 shows the results obtained. The 5 arrows reading from left to right represent the addition to the bath of $\frac{1}{100}$th of a unit, $\frac{1}{50}$th of a unit, $\frac{1}{10}$ of a unit, $\frac{1}{2}$ of a unit and 1 unit of pitocin. As in the previous experiment there was no response from the strip taken from the upper uterine segment.

An important difference between the response of the lower uterine segment to pitocin and the response to pitressin must now be considered in detail. Whereas the strip from the lower segment reacted to pitressin in amounts as small as $\frac{1}{50}$th of a pressor unit, there was no comparable response to pitocin until $1\frac{1}{2}$ of an oxytocic unit had been added to the bath. In other words, in this experiment, unit for unit, pitressin was about 25 times more effective than pitocin in causing the isolated human pregnant uterus to contract. Pitocin, however, contains a residual pressor content equivalent in pressor units to $\frac{1}{25}$th of the oxytocic activity in oxytocic units; these results could therefore be explained by assuming that most if not all of the oxytocic activity,

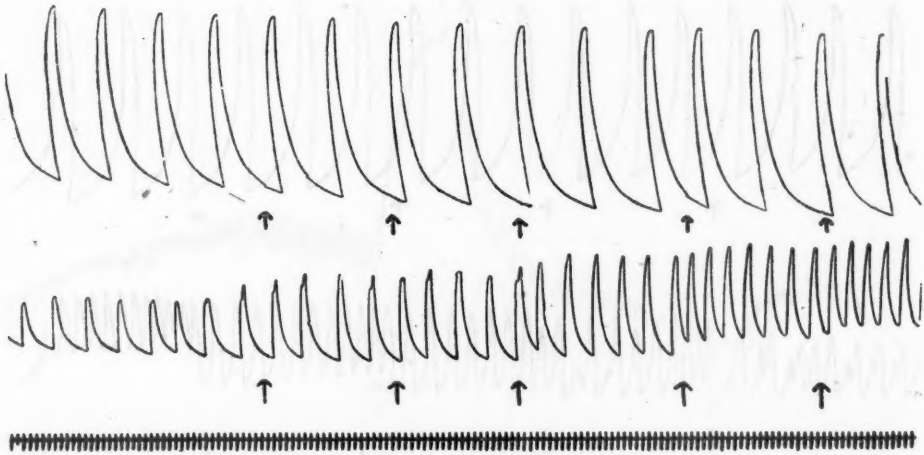

FIG. 4.

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the same uterus as in Figure 3, showing the effect of pitocin on the lower segment, and the absence of effect on the upper segment (human uterus).

1st arrow.....1/100th of a unit of pitocin
2nd arrow.....1/50th of a unit of pitocin
3rd arrow.....1/10th of a unit of pitocin
4th arrow.....1/2 of a unit of pitocin
5th arrow.....1 unit of pitocin

for the isolated human uterus, is associated with the pressor principle.

Muscle strips from both the upper and lower uterine segments of the same uterus, at or shortly before term, have been available for study on only one other occasion. Figure 5 shows the results obtained, the upper tracing corresponding to the upper segment and the lower tracing to the lower segment. Reading from left to right, the first, second, fourth and fifth arrows mark the addition to the bath of pitressin, whereas the third arrow marks the addition of pitocin. Each time pitressin was added there was a definite motor effect in the lower tracing (lower segment) but the addition of pitocin produced no such effect. The pitressin used for the last addition (fifth arrow) was the ordinary commercial preparation; the response is seen to be similar to that following the addition of the more highly purified material. As before there was no response from the strip obtained from the upper uterine segment.

The possibility was now considered that pitressin might have acted by inhibiting the action of pitocin. The addition of the latter preparation in increasing amounts was therefore made first, to a strip from the lower uterine segment of another uterus. The result is seen in Figure 6. The first four arrows, reading from left to right, correspond to the addition to the bath of $\frac{1}{200}$th of a unit, $\frac{1}{100}$th of a unit, $\frac{1}{10}$th of a unit and $\frac{1}{2}$ of a unit of pitocin. There was no suggestion of a motor response until $\frac{1}{2}$ of a unit had been added. The fifth arrow corresponds to the addition of $\frac{1}{2}$ of a unit of pitressin. The increase in tone after the pitressin was so pronounced that it

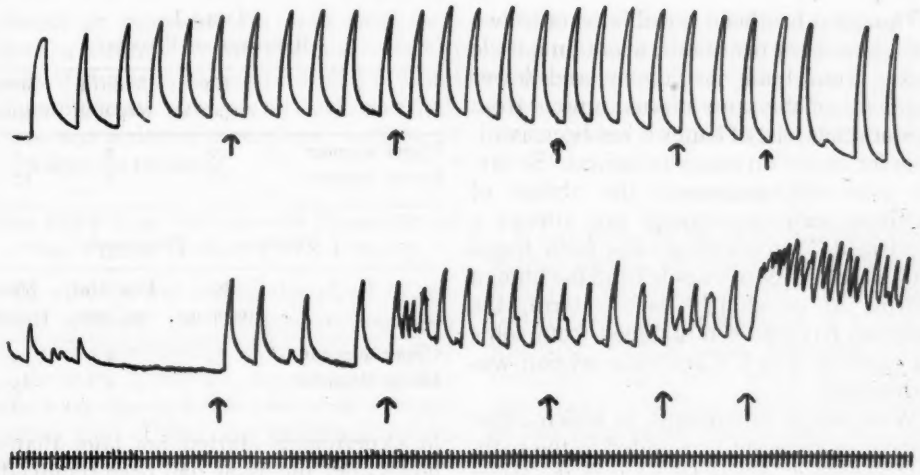

FIG. 5.

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the one uterus showing the effect of pitressin and pitocin on the lower segment and the absence of effect on the upper segment (human uterus).

1st arrow.....1/100th of a unit of pitressin
2nd arrow.....1/10th of a unit of pitressin
3rd arrow.....1/10th of a unit of pitocin
4th arrow.....1/10th of a unit of pitressin
5th arrow.....5 units of commercial pitressin

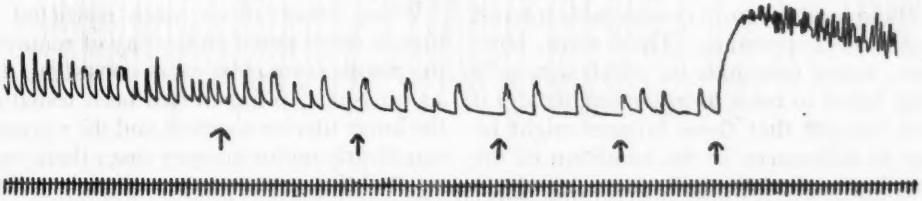

FIG. 6.

A comparison between the effect of pitocin and pitressin on a muscle strip from the lower uterine segment (human uterus).

1st arrow.....1/200th of a unit of pitocin
2nd arrow.....1/100th of a unit of pitocin
3rd arrow.....1/10th of a unit of pitocin
4th arrow.....1/2 of a unit of pitocin
5th arrow.....1/2 of a unit of pitressin

appears reasonable to state that the slight motor effect following the addition of $\frac{1}{2}$ of a unit of pitocin was proportional to, and could be due to its pressor content—equivalent to $\frac{1}{80}$ th of a pressor unit; an amount which on other occasions was known to have provoked a similar minimal motor response.

Though it has been possible on only two occasions, at or near term, to obtain muscle tissue from both the upper and lower segments of the same uterus, muscle from one or other part of a uterus has been available for study on many occasions. So far, on over 175 occasions, the action of pituitary extracts—though not always a "purified" preparation—has been tested on isolated strips of muscle from the human uterus, at or shortly before term, the material having been obtained from some 20 cases in which Caesarean section was performed.

When every experiment, in which either pitocin or pitressin was added to the bath, was analysed, it was found that the lower uterine segment, tested 102 times, showed a motor response on 53 occasions (52 per cent), whereas motor effects were observed from the upper segment, tested 70 times on only 9 occasions (13 per cent).

Results of Experiments on Muscle Strips Tested soon After Removal.

These results were of considerable interest and some importance. There were, however, many occasions on which a muscle strip failed to react to any stimulus and it was thought that these failures might be due to differences in the condition of the muscle samples obtained, and particularly to the time between their removal and their use for experimental purposes. A more detailed study showed that, almost without exception, the non-reactive muscle strip had been tested many days after its removal at operation. A further analysis was therefore made of results obtained from pieces of muscle tested within 3 days of removal, and also of the results obtained from strips suspended in the bath within 2 hours of removal. Table I shows the reaction of strips from the upper and lower uterine segments to pitressin and to pitocin

Table I.

Response to Pitocin

	No response	Doubtful response	Motor response
Upper segment ...	20	3	3
Lower segment ...	17	2	17

Response to Pitressin

	No response	Doubtful response	Motor response
Upper segment ...	23	4	3
Lower segment ...	3	4	25

in experiments started not later than 48 hours after the tissue had been removed at operation. It will be seen that the lower uterine segment showed a motor response to pitressin on 25 out of 32 occasions (78 per cent) whereas the response of the upper segment to pitressin was motor on only 3 out of 30 occasions (10 per cent). Even though the figures are comparatively small this difference in reactivity of the two parts of the uterus is significant.

When observations were restricted to muscle strips tested on the day of removal, the results were even more consistent. On 14 occasions, pitressin had been tested on the lower uterine segment and the response was clearly motor in every case; there were no doubtful responses even though as little as $\frac{1}{100}$th of a unit had been added to the bath. On 13 occasions pitocin, $\frac{1}{10}$th of a unit or more had been added to the bath; the response was motor on 11 occasions, the degree being more or less proportional to the known pressor content, assuming no activity from the oxytocic fraction *per se*. In 2 cases out of the 13 there was no response to $\frac{1}{10}$th of a unit of pitocin. On 6 occasions less than $\frac{1}{10}$th of a unit of pitocin was added to the bath; in no case was there a motor response. On 24 occasions the upper uterine segment was tested with either

pitocin or pitressin and only twice was there a definite motor response—after 3 units of purified pitocin and after ½ of a unit of commercial pitocin; on four occasions there was a doubtful response, and on 18 occasions no response.

The Effect of Pitocin and Pitressin on the Virgin Guinea Pig's Uterus.

In view of the results described in previous sections, the two preparations used in these experiments were now re-tested, in the same apparatus, by comparing their effect on the isolated uterus of a virgin guinea pig. Using the technique recommended by Burn[12] it was found that the pitocin was *at least* 5 times more powerful as a uterine stimulant than the pitressin; and comparing the minimal amounts that would produce a motor response the pitocin had *at least* 10 times the uterus stimulating activity of the pitressin (Fig. 7) The fractions thus responded normally to the orthodox method of standardization.

Discussion.

It has been shown that isolated strips of human uterus, obtained during the operation of Caesarean section at or shortly before term, and suspended in a bath of warm oxygenated Locke's solution, exhibit rhythmic contractions which vary in their extent and pattern according to the texture of the individual muscle strip and other factors already mentioned. The response to pitocin and to pitressin of different muscle strips from the same part of the uterus was similar even though the patterns

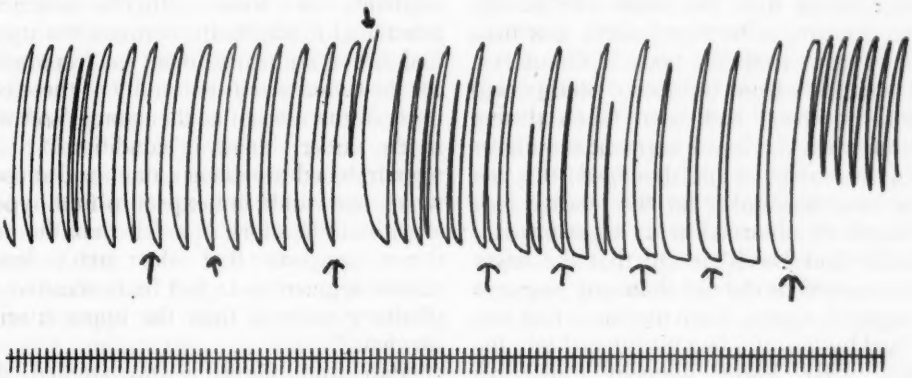

Fig. 7.

A comparison between the effect of pitocin and pitressin on the isolated virgin guinea-pig uterus.

1st arrow.....1/100th of a unit of pitocin
2nd arrow.....1/50th of a unit of pitocin
3rd arrow.....1/20th of a unit of pitocin
Solution changed
4th arrow.....1/50th of a unit of pitressin
5th arrow.....1/20th of a unit of pitressin
6th arrow.....1/5th of a unit of pitressin
7th arrow.....1/2 of a unit of pitressin
8th arrow.....1/20th of a unit of pitocin

recorded may have varied within wide limits; no demonstrable difference was observed between the response of strips cut from the same uterus, to include a preponderance of circular or a preponderance of longitudinal fibres. When, however, muscle strips from the upper uterine segment and muscle strips from the lower uterine segment were compared by suspending them in the same bath and subjecting them to the same concentration of pituitary extracts, striking differences were observed. Those from the lower segment, immediately after their removal from the body, were found to be sensitive, always reacting to pitressin with a motor response: in contrast, those from the upper uterine segment showed no such response to pitressin.

Robson[13] found that the reactivity of muscle strips from the lower uterine segment appears to be significantly less than that of strips from the body of the uterus. All his strips from the lower uterine segment, however, had been taken during labour when the lower segment may have been overstretched and damaged; this fact may have accounted for the relative lack of reactivity observed in his experiments.

Adair and Davis[9] found that the lower uterine segment did not show any response to oxytocic agents, when uterine action was studied by use of a bag introduced into the uterus after lower segment Caesarean section. Their failure to get any response from the lower segment may have been due to this part of the uterus, overstretched after the delivery of the child through it, being temporarily unable to retract down on the intrauterine bag. Possibly they would have been able to demonstrate motor effects if, as the bag was withdrawn from the upper segment, its size could have been increased to fit the stretched lower segment. The operative trauma, the suture line, and the anaesthetic may also have adversely influenced their results. As their experiments were made on the uterus *in situ* it must be considered whether the response of the isolated muscle strip from the human uterus, as used in this investigation, may be taken to indicate what happens in the intact organ. When the effect of the drug is a direct one, as appears to be the case with pituitary extracts, the reactions in the differing conditions are likely to be the same. Strips from the upper and lower segments were obtained for this investigation under conditions which, though comparable, were not exactly similar, the individual muscle fibres having been stretched more during lower that during upper segment Caesarean section, because of technical differences in the two operations. Either this slight additional irritation to the lower segment, or some hitherto unknown functional dissimilarity between the upper and lower segments, must be responsible for the difference in reactivity of these two parts of the uterus, as the comparison was made under identical conditions.* An overstretched muscle is a damaged muscle which one would not expect to find hypersensitive; therefore it is felt that the evidence suggests that the intact lower uterine segment is in fact more sensitive to pituitary extracts than the upper uterine segment.

Adair and Davis,[9] who studied the uterine response following lower segment Caesarean section, concluded that so far as human beings were concerned, they could not distinguish between the action of pitocin, pitressin and pituitrin. Indeed they found that pitressin provoked as powerful a response as pitocin and pituitrin even though less had been injected. Some years later, Adair and Haugen[6] using isolated human uterine muscle strips recorded that the response was usually greater after the addition to the bath of

* See additional note at end.

pitressin than after the addition of pitocin; on several occasions they found that a strip of muscle which did not react to pitocin reacted to pitressin. A search of the literature has not revealed any satisfactory explanation of these observations, which have been repeatedly confirmed during the present investigation. It has now been shown that on the isolated full-time pregnant human uterus, pitressin appears to be approximately 25 times more active than pitocin; and that any oxytocic activity the latter preparation may have is not more than would be expected from the pressor substance in it, assuming this to be the principle entirely responsible for stimulating the human uterus.

When the isolated uterus of a virgin guinea pig was tested under similar conditions in the same apparatus the actions were reversed and pitocin was found to be at least 10 times more powerful as a uterine stimulant than pitressin. In other words it may be said that the pituitary fraction, chiefly responsible for the motor effect on the isolated virgin guinea pig's uterus and known as pitocin, has a negligible effect on the isolated full-time pregnant human uterus, compared with that of the fraction that raises the blood-pressure of an anaesthetized dog, known as pitressin. This reversal of effect is clearly of the greatest importance, as extracts of the posterior lobe of the pituitary, perhaps to be used in the induction of labour in women, are at present being standardized for potency against the uterus of the virgin guinea pig.

As the pressor and anti-diuretic properties of the posterior lobe of the pituitary appear to be concentrated in pitressin and as this has now been shown to possess a greater oxytocic activity for the isolated full-time pregnant human uterus than pitocin, it might be claimed with some justification that, in so far as the human subject is concerned, the evidence suggests that a separation of the pressor and anti-diuretic principles from the oxytocic principle has not been effected. Pitocin however has a greater oxytocic activity than pitressin on the isolated virgin guinea pig uterus. It appears, therefore, that two powerful oxytocic principles, differing in their biological activities, have been obtained from posterior pituitary extracts; the one, concentrated in pitocin, provoking a motor response from the isolated uterus of a virgin guinea pig, but having little effect on the isolated muscle strip from the human pregnant uterus: the other, concentrated in pitressin, provoking a motor response from the isolated human pregnant uterus but having little effect on the isolated virgin guinea pig's uterus. Whether these two principles are similar or dissimilar in composition is a question that cannot as yet be answered.

It is difficult to avoid the conclusion that the further attempt to separate the active principles with a view to obtaining one which contains the oxytocic principles for use in human obstetrics, will be doomed to failure unless controlled by experiments on the human uterus or on the uterus of an animal which shows the same qualitative response to pituitary extracts.

Summary and Conclusions.

1. The reactions to pitressin and to pitocin of muscle strips from the upper and lower segments of the human pregnant uterus, at or shortly before term, have been compared.

2. Muscle strips from the human lower uterine segment are much more sensitive to posterior pituitary extracts than strips from the upper segment.

3. Pitressin has been found to be approximately 25 times more powerful a stimulant for the human uterus than pitocin: but for

the virgin guinea pig's uterus, under the same conditions pitocin was found to be at least 10 times more powerful a stimulant than pitressin. The significance of this has been briefly discussed.

Acknowledgments.

I wish to express my gratitude to Professor J. A. Gunn, Director of the Nuffield Institute for Medical Research, for his constant help and encouragement; without his consent and tuition this investigation would not have been possible. I am also indebted to Professor Chassar Moir, Mr. J. A. Stallworthy, and Mr. G. C. Lennon for valuable criticism and for supplying me with pieces of uterus from cases under their care; to Professor J. Y. Bogue, for his advice and help on technical matters; and to the two laboratory assistants, Maurice Tuckey and Frank O'Connor for their ready assistance.

Additional Note.

Since writing this paper further observations have been made:

1. Further study of the reaction to pitocin and pitressin of isolated strips of the lower segment of the human full-time pregnant uterus has not revealed any difference between those cut before delivery of the child and those cut after the delivery of the child.

2. Two other pituitary preparations (Pitressin Rx 097376, Pitocin Rx 097796) kindly supplied by Messrs. Parke, Davis & Co. have been tested on isolated strips of the full-time pregnant human uterus. The Pitressin was found to have a greater activity than pitocin the effect being largely on the lower uterine segment. This was in agreement with the observations already made and described in the present paper.

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Antenatal Thrombophlebitis

BY

J. PRESTON MAXWELL, M.D. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G.

ANTENATAL thrombophlebitis is a rare disease, and the prognosis in these cases is in doubt, owing to the paucity of material from which to form a definite judgment.

Browne[1] speaks thus on the matter: "This is a rare complication of pregnancy—the patient is usually a multipara—varicose veins predispose to it. It may, however, start for the first time in pregnancy, and in an apparently normal patient, and affect the iliac, femoral, or saphenous veins, usually of one side. Neither is there any special predisposition to the development of phlegmasia in the puerperium."

The following case is presented as an addition to our knowledge of the condition:

Mrs. K.B., a 4-gravida, was admitted to the White Lodge Hospital (E.M.S.) on May 5th, 1942, suffering from antepartum thrombosis of the superficial saphenous system in both thighs. This thrombosis extended up to the saphenous opening on both sides, and down as far as the knee. Not only was the great saphenous vein palpable, as a hard tendon cord, but the lateral branches were also affected. There was practically no oedema of the lower legs and feet, but she had already been in bed for one week. The condition started with redness and pain on the inner surface of both thighs. A cause was not found. The patient was in good health, the blood-pressure normal, and there were no prominent varicose veins in either leg. A catheter specimen of urine showed a faint cloud of albumin, there were no casts, but a few leucocytes. Culture showed a very scanty growth of bacillus coli and staphylococcus albus. Her blood sedimentation rate was 1st hour, 27 mm.; 2nd hour, 60 mm.; her blood count was normal, and she was not anaemic. A septic focus was not found though a careful search was made.

The pregnancy was a twin one. She was kept at rest in bed, and by the middle of June the thrombosis had disappeared, and there was nothing to note about the legs, save a slight oedema of the lower leg. A trace of albumin persisted, and the blood-pressure was normal. She was then allowed up and about, and was walking steadily and well.

On July 13th, 1942, a fortnight before her expected date, she went into labour and was delivered of twin girls; the first presenting by the head, and weighing $5\frac{3}{4}$ pounds; the second presenting by the breech, and weighing $5\frac{1}{4}$ pounds. Both children progressed well. The placenta was a single one; a single chorion and two amnions. There was no excessive haemorrhage. The patient made a rapid and satisfactory recovery without incident, and she left the hospital well on the 18th day of the puerperium; there was no sign of trouble in the legs.

She was able to nurse both children, and was so doing 6 weeks later when she was in good health. The children were progressing normally. Her previous pregnancies had been:—

(1) A twin one (girls), carried 5 months only.
(2) A 9 pound girl, alive and well, now aged 7.
(3) A 9 pound girl, alive and well, now aged 5.

The interesting points of the case are the very marked thrombophlebitis, and the fact that there was no sign of recurrence after labour. The only treatment given was a capsule of adexolin twice a day, and a tablet of ascorbic acid thrice daily.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

D.R.C.O.G. Examination, March 1943.

THE following candidates satisfied the examiners for the Diploma of the College:

Harrison Broadbent	Jean Ann Forbes	A. S. Minabbawy
Walter Calvert	Agnes J. M. Gilruth	Joyce G. Neil
Nora H. C. Clarke	Irene D. M. Hastilow	Erica M. Roberts
Frank Blair Davidson	Mary M. Lynch	Edith Taylor
Gerald S. W. Evans	Irene E. Howorth	Mary U. Wilkin.

The Quarterly Meeting of the Council was held on Saturday, May 1st, 1943, in the College House, with the President, Sir William Fletcher Shaw, in the Chair.

The Honorary Fellowship of the College was conferred on Sir Wilson Jameson, the Chief Medical Officer of the Ministry of Health, in recognition of his services to obstetrics and gynaecology.

The following were formally admitted to the Fellowship by the President:

Gladys Hill — Norman Lewis White

The following were formally admitted to the Membership by the President:

Janet Elizabeth Bottomley	Louis Resnick
Phillis Dingle	Gordon Short Sturtridge
Marjorie Olive Dunster	Kenneth Gordon Patrick Worner

The Annual General Meeting of the College was held on Saturday, May 1st, 1943, in the College House, with the President, Sir William Fletcher Shaw, in the Chair.

The following were elected to Council in place of those retiring by statutory rotation:

Representatives of the Fellows:

Arthur James McNair — John Chassar Moir

Arthur Alexander Gemmell — Robert Henry Joseph Mulhall Corbet

Representatives of the Members:

Bryan Leslie Jeaffreson — James Sinclair Quin

The Council was gratified to receive the gift of £1,000 from a Fellow of the College who wished to remain anonymous. It has been given to commemorate the Presidency of Sir William Fletcher Shaw and the honour of Knighthood conferred on him by H.M. the King, and the interest from the gift will form a scholarship to be awarded triennially for research.

BOOK REVIEWS

"A Textbook of Gynaecological Surgery." By Sir Comyns Berkeley and Victor Bonney. Fourth edition. 574 original drawings by Victor Bonney and 17 coloured plates. 1943. Cassell & Co., Ltd. London, Toronto, Melbourne and Sydney.

The idle turning of the pages of the new edition of this famous gynaecological operative surgery, and a glance at the illustrations which so lavishly adorn the book are sufficient to evoke sentiments akin to those aroused in Keats, prompting the famous lines in "On Reading Chapman's Homer." The surgeon who reviews this work still recalls the thrill of pleasure and admiration produced by the appearance of the first edition and tenders his tribute to the authors for the immense aid which the book has rendered not only to gynaecological surgeons, but also to those whose surgical labours range over a wider territory of the body than the female pelvis.

A feature of the present edition is the conservative attitude adopted in the treatment of many of the problems of pelvic pathology. A growing appreciation of the manifold functions of the ovary has led gynaecological operators, not too soon, to exhibit a greater reluctance to remove these structures, and the reproach is at length removed from those who practise this important branch of surgery that "a snowflake in hell" has a better chance of survival than an ovary in a gynaecological operating theatre.

This conservatism has also extended to the uterus in the treatment of many myomata and also to the diseased or damaged Fallopian tube. One of the two authors performed myomectomy for fibroids 379 times with a lower mortality than the microscopic death-rate attending sub-total hysterectomy, and of those patients within the child-bearing age desiring children after this operation, no less than 38 per cent conceived, and 75 per cent of the children were born normally.

The anxieties attendant upon the Baldwin-Mori operation for absence of the vagina have been removed by McIndoe's plastic operation, and although the authors describe in detail the former operation they make it clear that it has been relegated to the limbo of the past by this new contribution from the plastic surgeon's art.

It is not within the province of the reviewer to enter into the debate between radiotherapy and the Wertheim operation for carcinoma of the cervix. Carcinoma of the cervix is a very common malady, the radium technique is very easy and yields results better than an imperfect radical operation; and there are few surgeons in the world who have had the experience of the Wertheim operation which the distinguished authors of this work enjoy. The operation is perhaps the most exacting of all gynaecological procedures, and to the surgical onlooker it would appear that the Wertheim operation which yielded such good results in the hands of Berkeley and Bonney at a mortality rate of 14 per cent in a long series is now likely to pass into desuetude.

No detail is omitted of the operative and non-operative methods required to deal with difficulties encountered during laparotomy or embarrassing the convalescence. One of the authors was among the pioneers of enterostomy for post-operative ileus; the technique of reimplantation of the sectioned ureter into the bladder is described and well-illustrated. The Paul-Mikulicz exteriorization type of large bowel resection is somewhat fashionable with abdominal surgeons just now, but the authors prefer end-to-end suture.

The patients of the two authors were never wont to grow much older during the progress of their operations; these surgeons learned from their master, Sir John Bland-Sutton, the importance of time, and their own mantle has descended upon many disciples. The speed of the modern gynaecologist contrasts with a slow school of surgery which has grown up and makes him a most valuable asset in the abdominal surgery of total war; many excellent cases already stand to their credit in this sphere of traumatic surgery.

Reference has already been made to the excellent illustrations for which one of the writers is responsible; these must have been a guide and beacon to many a less experienced operator, and must have kept many a surgical fee out of the pockets of the authors.

G. GORDON TAYLOR

"Midwifery for Nurses." Third edition. By DOUGLAS MILLER, M.D., F.R.C.S. (Edin.), F.R.C.O.G. Edward Arnold and Co. 7*s*. 6*d*.

THIS book is a useful introduction to the theory and practice of midwifery. The fact that throughout the book the writer refers to the nurse and never to the midwife leads one to presume that it is intended for the maternity nurse and not the practising midwife; since the information it contains is insufficient to meet all the requirements of the pupil studying for the Central Midwives Board first and second examinations, or to serve as a reference book for the qualified midwife.

Some of the statements regarding treatment are misleading. Removal of retained membrane from the uterus immediately following the 3rd stage of labour is contrary to the teaching in most training schools. Sylvester's method of artificial respiration is generally considered quite unsuitable for the asphyxiated baby, and the use of a warm bath in asphyxia pallida. Experience does not support the assertion that immersion of the baby at the daily bath is liable to cause infection of the cord.

In the section on abortion the period of viability is given as the 30th week of pregnancy, whereas the legal definition of abortion is the termination of pregnancy before the 28th week, and this is accepted by Insurance Companies in respect of the payment of the maternity benefit.

The section on the physiology of labour is particularly clear with the diagram describing the dilatation of the cervix, so also is the chapter on the clinical course of normal labour. It is disappointing that in the management of normal labour reference is not made to the use and action of sedative drugs which a midwife, acting as such, may administer.

E.A.C-K., S.R.N., S.C.M.

REPORTS ON HOSPITALS AND DEPARTMENTS OF PUBLIC HEALTH

THE REPORT OF THE ROTUNDA HOSPITAL FROM 1ST NOVEMBER, 1940, TO 31ST OCTOBER, 1941.

THIS report which appears with unfailing regularity hardly needs introduction. The high standard set by his predecessors has undoubtedly stimulated the new Master, Dr. Falkiner, and we congratulate him on his achievement. The report records with regret the death of Sir William Smyly, who had maintained a life-long interest in the Rotunda, and whose Mastership coincided with the changes that ensued as a result of the introduction of asepsis and antisepsis into obstetrics. A richly deserved tribute is paid to Dr. Davidson, the retiring Master. Structural additions to the hospital include a new lecture room, and a new pathological laboratory, the old having been refitted as a research department. A new department for premature and sick babies has been completed, an example all maternity units would do well to copy in an effort to lower the grievously high mortality that still prevails among the premature. The report although principally concerned with the maternity work, includes an account of the work of the gynaecological paediatric, pathological and X-ray departments.

The total number of attendances in the Out-patient Department shows a decrease to which no particular significance may be attached. An investigation of the Wassermann reaction in 800 consecutive cases is mentioned. Surely the time has come for all antenatal patients to have their blood reaction tested? The significant fact that 50 cases of syphilis were treated suggests the urgent need for the adoption of this test as a routine investigation.

Mention is made of the excellent work done by the Social Service Department, surely justifying extension of these services which are only restricted in most hospitals by financial considerations. The In-patient Department admitted 3,896 patients, of whom 3,536 were delivered, 12 mothers died. The district deliveries numbered 1,530, none of which ended fatally, a tribute to the excellence of the domiciliary practice.

There follows a most interesting account of the various presentations and obstretic abnormalities, and mention is made of the treatment carried out. One is sorely tempted to make adverse comments when the procedure adopted is not in keeping with one's own methods, while a similar urge to applaud is felt when agreement with one's view is apparent. This is exampled by one's horror at the use of Bougie induction, particularly in cases of disproportion, and more so when lower segment section was required on one occasion to deliver the patient. Unanimity over the restricted use of quinine for medical induction restores good feeling! Similar examples could be repeated over and over again, but any obstetrician anxious to improve his art is urged to read the report in its entirety and then to search himself. Would he list albuminuria as an indication for delivery by the forceps? Primary inertia is not defined in terms of hours in the 1st stage of labour, but merely as prolonged labour. The conservative attitude described is to be commended, but no mention is made of any specific remedies such as the oestrogens. Mention is not made of the dietetic treatment of pre-eclampsia, still referred to as albuminuria. Has the high protein, salt-free diet not found a place in the Dublin treatment? Energetic and early treatment with the sulphanilamides appears to have been successful in the treatment of puerperal sepsis; no deaths occurred in spite of several instances of haemalytic streptococcal infection. The maternal mortality for booked cases was 0.11 per cent which contrasts markedly with 1.13 per cent for emergency cases. In the gynaecological department there were 617 admissions, and of these 553 were operated upon. We note that Wertheim's hysterectomy still has a place in the surgical activities of the Rotunda. The

appointment of a blood-transfusion officer has many advantages, but it limits the opportunities for junior residents to give transfusions, experience which might prove invaluable in their future practice. Dr. Falkiner concludes his summary of his year's work with a well-deserved tribute, both medical and nursing, the excellent standard of past years having obviously been maintained.

Dr. W. R. F. Collis has contributed a short account of the paediatric department. Mention has already been made of the opening of the new nurseries exclusively for the treatment of abnormal babies. This is an important advance, and we hope that the more complete records to be available soon, will demonstrate the value of this step. The pathological department's statistics indicate the increasing value of laboratory investigations in obstetrics and gynaecology. Comment has already been made on the need for instituting a routine Wassermann reaction. The report concludes with a list of the number and variety of radiological examinations performed, further evidence of the value of such a department in all modern maternity departments.

REGISTRAR'S REPORT, LIVERPOOL MATERNITY HOSPITAL, YEAR ENDING DECEMBER 31ST, 1941.

THIS report reflects the effect of enemy action on the work of a large maternity hospital, namely a decrease in the total number of patients, but a greatly increased number of emergency admissions. The statistical summary states that 2,624 patients were attended by the hospital, 955 in their own homes (the latter figure corresponds with the figure given in the district report), and 1,669 in hospital. The latter figure is then analysed into 1,502 patients booked, and 617 emergencies, which is clearly inaccurate. It would seem that the figure should be 1,025 and not 1,502. The tabulated records of the various abnormalities provided some points of interest. In the section on heart-disease, Caesarean section was the treatment in 25 per cent, the actual number of cases being small, but the percentage is relatively high. Colonic lavage, once advocated in Dublin, and more recently almost renounced by them, is employed in the treatment of eclampsia, nevertheless the patients recovered. A set technique is described for breech-delivery, and maintenance of traction after the birth of the buttocks is included; surely traction is to be avoided, particularly at this stage. A breech mortality of 7.4 per cent is impressive until the total figure of 25 per cent is arrived at by means of a little mental arithmetic. In the copy of the reports received, page 11 must be looked for between pages 44 and 45. A maternal mortality of 0.4 per cent for booked cases is relatively high, but it is unusual to encounter 2 cases of liver atrophy in 1,500 cases. Details are given of all the fatal cases, one attributed to obstetric shock is very puzzling, and makes one wonder whether it is advisable to give such a quantity of blood (3 pints) to a patient in whom there was no bleeding. The report concludes with a paediatric section. It would be interesting to know if the Rhesus Factor was investigated in the 3 cases of icterus gravis. Perhaps it is not too late now to determine the parental reactions. We are not familiar with the heading "genital crisis," which seems to include mastitis, hydrocele, and malaria within its scope.

Review of Current Literature

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab.), F.R.C.S., F.R.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges.

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world; owing to the war many journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received. At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed. Arrangements are also made to include abstracts of important articles on borderline subjects, such as Physiology, Biology, and Biochemistry.

LIST OF ABSTRACTORS

J. LYLE CAMERON, F.R.C.S.
W. E. CROWTHER, M.B.
R. H. B. ADAMSON, M.D.
B. JEAFFRESON, F.R.C.S.
P. MALPAS, F.R.C.S.
T. N. A. JEFFCOATE, F.R.C.S.
MEAVE KENNY, F.R.C.S.
JANE H. FILSHILL

The Canadian Medical Association Journal

Vol. xlvi, March 1942, No. 3.

*An improved radical technique for carcinoma of the external genitalia in the female. H. W. Johnston.

AN IMPROVED RADICAL TECHNIQUE FOR CARCINOMA OF THE EXTERNAL GENITALIA IN THE FEMALE.

Carcinoma of the external genitalia is a rare disease and is confined almost entirely to elderly women. The growth begins as a nodule, a wart or an ulcer, and in more than 50 per cent of cases it follows leukoplakic vulvitis.

Treatment demands removal of the primary growth and the lymphatic glands which drain the vulva. The lymphatic drainage is very rich, anastomosing freely, and a growth on one side may invade the glands in both inguinal regions.

There are two groups of inguinal glands, superficial, and deep. The superficial glands are from 10 to 20 in number, lying immediately below Poupart's ligament. Several of these lying over the fossa ovalis are usually very large. The chief drainage into these glands is from the vulva. The deep glands, usually known as the glands of Cloquet, lie medial to the femoral vein. They receive lymph from the superficial glands and directly from the regions of the clitoris and the urethra. Their removal is usually difficult and was formerly considered in many cases to be impossible. Bassett introduced the technique of dividing Poupart's ligament to expose these glands and facilitate their removal. There is, however, some difficulty in restoring Poupart's ligament afterwards.

In thin patients palpation and removal of these glands is simple. In fat patients it is essential to remove a large T shaped mass of fat which enmeshes the glands. The horizontal part of the T lies below Poupart's ligament, the vertical part over the saphenous opening.

The majority of patients with cancer of the vulva are poor operation risks, and a procedure is here described which permits speed and extensive removal of the primary growth with its draining lymphatics.

An incision is made an inch below Poupart's ligament, extending from a point below the pubic spine to a point below the anterior superior iliac spine. The skin on each side of the wound is

dissected free from underlying fat and well retracted. This exposes in the groin a mass of fat adherent to the abdominal fascia above, Poupart's ligament centrally, where the adherence is very dense, and to the fascia lata below. This mass of fat is dissected with the aid of scissors from the underlying structures. Usually the dissection is started at the upper part, carried downwards and then medially. As the fat is raised from its bed and drawn medially, the long saphenous vein will be clamped and divided, together with another small vessel penetrating the fascia lata. This mass of fat is drawn medially, exposing the saphenous opening, which is cleared of fat and glands by gauze dissection. All the fat as far as the symphasis pubis must be removed at the same time, together with the areolar and fatty tissue of the outer part of the vulva, where there are many small glands. The mass of fat will have the appearance of the letter T, the horizontal part being the tissue which occupied the region above and below Poupart's ligament, while the vertical limb of the T will be the tissue lying along the saphenous vein. Three superficial vessels will require division and ligation: the superficial epigastric, the superficial circumflex iliac, and the external pudic. The long saphenous vein will also be divided and ligated, as this permits a freer exposure.

The femoral vein is drawn gently outward with the left index finger and Gimbernat's ligament is divided with a pair of curved scissors, thus exposing the deep inguinal glands. Occasionally an abnormal obdurator artery will be present; it runs downwards along the front of Gimbernat's ligament at about its centre. The possibility of its presence must be kept in mind.

The deep inguinal glands lying medial to the femoral vein are removed with the finger, assisted by traction with a pair of ring forceps. The inguinal ring is also explored, as on rare occasions a gland is found in this region. Through the ring also the peritoneum may be lifted upwards and further removal of areolar tissue effected.

The boundaries of the femoral ring are defined, the divided Gimbernat's ligament repaired by suturing the part of Poupart's ligament medial to the femoral vein to the medial portion of the ileopectineal fascia. Its closure is completed with three or four interrupted stitches. All these manipulations should be conducted with great care to avoid not only penetrating the femoral vein, but exerting undue prolonged pressure upon it, as this might cause stasis and thrombosis. The inguinal ring is closed with interrupted stitches, and the edges of the deep fascia are approximated. The skin wound is closed with one continuous and four or five interrupted sutures of black silk. A small drainage tube is left in the inner end of the wound, as exudation of serum is always copious. The same procedure is carried out on the opposite side.

The patient is placed in the lithotomy position and the vulva is excised. Two oval incisions are made, one around the entrance of the vagina and passing in front of the meatus urethrae, after leaving a fairly wide margin of mucosa, the other, and outer incision passes wide of the growth around the whole vulva. A bridge of skin may be left across the perineum, except in cases of leucoplakia. The greater and lesser labia, the vestibule, the clitoris and the mons veneris are dissected free and removed. The dorsal vessels of the clitoris are of considerable size and must be carefully ligated. Freely oozing areas are underrun with catgut and tied.

The wound in the vulva is closed with interrupted stitches of silkworm gut and a few catgut. In front of the urethra the skin edges on each side are approximated, while behind the urethra the cut skin is sewn to the divided edge of the vagina. It there is difficulty in bringing these edges into coaptation, under-running the skin, or in the worst cases, lateral incising of the skin will suffice to effect adequate relaxation. The sutures round the urethral orifice require careful placing.

When the urethral orifice is involved, a modification of the anterior part of its inner incision will be required. The anterior part of this incision does not pass in front of the urethra, but through the vaginal wall behind it and the urethra is transected at about its centre, permitting removal of the greater portion of this tube. Much free oozing will result and is controlled by passing surrounding sutures of catgut. A new meatus is fashioned by suturing the mucosa of the urethra to the anterior part of the vaginal mucosa, which has been cut with convexity forwards, so as to permit readily of reconstruction. Undercutting of the vaginal mucosa may occasionally be neces-

sary to avoid tension. Black silk is the best material for sutures.

Eighteen very excellent serial drawings to illustrate the steps of the operation are included.

Vol. xlvi, June 1942, No. 6.

*The treatment of acute and chronic salpingitis. A. B. Nash.

TREATMENT OF ACUTE AND CHRONIC SALPINGITIS.

The commonest cause of pelvic inflammation is the gonococcus. This organism has a predeliction for mucous surfaces and for the sub-epithelial tissues of glands. Here these organisms retain their infective potentialities for a long time, even after all external signs have ceased to be in evidence. Secondary pyogenic infection is liable to occur. It is this persistence of the gonococcus which causes recurring attacks of salpingitis, so that the acute stage may pass into the chronic phase, which is so liable to be attended by occlusion of the Fallopian tubes, damage to other structures and loss of function. It is important, therefore, to treat adequately the primary infection in the cervix.

When there is acute infection of the genital tract, the patient should be kept in bed, and examination and the use of instruments must be strictly limited, as the passage of specula and the application of medicaments to any part of the genital tract will not only fail to eradicate the disease in the lower tract, but will increase the chances of its spread to the Fallopian tubes. Even the use of sulphonamides has not yet been shown to eradicate the disease so quickly and completely that these precautions mentioned may be neglected with safety. It is no less important to enjoin strictly total continence, absence from alcohol, excitement, exposure to cold, physical exertion and fatigue. This applies particularly to a time near the menstrual period. These are factors contributing greatly to the occurrence of salpingitis. The case, however, must not be regarded as hopeless with regard to preservation of child-bearing function. There is a tendency for acute salpingitis to subside spontaneously, provided that no fresh infections are superimposed, and that the lines of treatment which have been given be followed. The beneficial effects of the sulphanilamides does not permit of laxity in employing these other methods of treatment. Both methods should be complementary, and rest in bed should be maintained for several days after the subsidenc of fever, pain, leucocytis, and increase in sedimentation rate, and it should be employed before, during, and after menstruation for the next two or three periods, at which times exacerbations are liable to occur. Fowler's position should be employed, ice bags applied to the lower abdomen, and pain and rectal tenesmus relieved by aspirin, codeine, or even tincture of opium.

Surgery has no place in the treatment of acute gonorrhoeal salpingitis, nor has the author any good opinion of the employment of heat as a therapeutic measure.

When the Fallopian tubes become sealed, there is little hope of retaining or retrieving fertility. Pylosalpinx, hydrosalpinx, tubo-ovarian abscess, extensive adhesions of the pelvic peritoneum and viscera are liable to occur. The ovaries may become involved in the inflammatory process. By this time the function of fertility must be regarded as destroyed. All this entails much suffering for the patient, and finally relief may be obtained by the employment of only the most radical type of surgery.

Whatever type of treatment is employed, it is liable to be minimized by physical exertion, alcohol, fatigue and sexual stimulation. The author is of the opinion that sulphanilamides in the chronic type of inflammation are of limited benefit, but heat by one of several methods is of some use. Non-specific protein therapy is of small value. It seems that time, patience, the avoidance of reinfection and aggravating influences are the most important elements in the treatment of chronic inflammation. None are easy to employ or to enforce, nor are they spectacular in their effects, and seldom are they utilized to their full extent.

Surgery should not be invoked until the methods cited have been given a full and competent trial, and especially until all inflammatory processes have subsided. But when resort is made to operative measures, these must be adequate. Half measures only entail the necessity of further operation. As the ovaries are usually seriously damaged, their conservation is liable to be followed by major menstrual aberrations. When no part

of an ovary can be conserved, the uterus is of little value and the cervix, it must be remembered, is chronically infected. Total hysterectomy, therefore, has to be considered.

Pyogenic salpingitis, acute or chronic, presents many of the problems already outlined.

Tuberculous salpingitis is not so uncommon as is usually believed. It is thought to occur as frequently as once in every 20 cases of salpingitis, although opinion on this point varies widely. When there is pronounced pulmonary tuberculosis the lung affection must receive first consideration. Sanatorium treatment must have its place. X-ray therapy in this condition is, again, a subject of extensive controversy. The difficulty of accurate diagnosis of tuberculous pelvic disease has a considerable bearing on radio-therapy. Most authorities agree that surgical treatment is indicated in the majority of cases. Pulmonary tuberculosis or extensive peritoneal involvement are contra-indications. Vaginal coeliotomy should not be performed as fistula formation is liable to result. Radical or limited surgery is again a matter of controversy, but apparently the majority of experienced surgeons favour extensive eradication. Ovaries at all affected are better removed. Dense and unyielding adhesions are almost certain to make any operation extremely difficult. Drainage of the peritoneum is condemned by the majority of surgeons. There are great difficulties in determining the extent of the disease, even when the organs are exposed to view and touch. Reproductive function is usually irrevocably lost long before the case is even diagnosed.

An eighteen-item bibliography is appended.

J. LYLE CAMERON

Medical Journal of Australia

September 7th, 1940.

*Haemorrhagic disease of the newborn.

October 19th, 1940.

Effects of testosterone propionate on pouch, scrotum, clitoris and penis of trichosurus vulpecula. A. Bolloger and A. Carrodus.

*Hydranencephaly. H. F. Bettinger.

The significance of the Aschheim-Zondek test in the early diagnosis of chorionepithelioma. W. G. Cuscaden and H. F. Bettinger.

May 2nd, 1942.

*Congenital lacunar skull. H. B. Bettinger.

May 23rd, 1942.

*Granulosa-cell carcinoma of the ovary, with the report of a case. R. Mackay.

June 13th, 1942.

Mesonephroma of the ovary. Current comment.

HAEMORRHAGIC DISEASE OF THE NEWBORN.

Under the heading of "Current Comment" a short review of the clinical manifestation of this condition is given. It is pointed out that in all such cases there is an excessive deficiency of prothrombin in the infant's blood, and this is thought to be the cause of the bleeding.

The ability of the liver to maintain the level of prothrombin in the plasma depends upon the presence of vitamin K in the diet and its absorbtion by the bowel. It is absorbed from the bowel only in the presence of bile salts.

The cause of physiological hypoprothrombinaemia of the newborn is obscure. It would appear that the placenta forms a barrier to the free passage of prothrombin from the maternal circulation to that of the foetus. High vitamin K feeding of the pregnant mother does appear to increase the amount of prothrombin in the blood of the newborn.

In an established case of haemorrhagic disease of the newborn the administration of vitamin K by mouth appears to be of value in the less severe case while more rapid increase of foetal prothrombin is secured by transfusion with normal adult blood.

HYDRANENCEPHALY.

Bettinger describes the case of a first-born child of a healthy mother of 21 years.

Labour was easy and spontaneous, and the foetus was, at birth, considered to be normal in all respects except that the cranial sutures were, if anything, a little wide apart. It took the breast like any normal child but its head was noticed to

feel cooler to touch than the head of other newborn babies. For five days it developed quite normally, then for two days it had a subnormal temperature and death occurred on the seventh day without any definite symptoms or signs.

On postmortem examination, when the skull was opened, the dura mater was very firmly attached to the inner surface of the bones and no trace of the cerebral hemispheres could be found. At this point it was decided to postpone further examination of the contents of the cranial cavity until the whole head had been hardened. After hardening the head was bisected. It was then seen that the cerebral hemispheres and the corpus callosum were completely absent; some mid-brain tissue was present below an obscuring membrane, but normal structures could not be recognized here. The pons, cerebellum and medulla oblongata were apparently normal. The thorax and abdomen contained no abnormality.

Histological examination of the cranial structures was not made as this could only have been carried out at the expense of destruction of the whole specimen.

The writer considers that in view of the presence of well-formed membranes and skull the condition must have arisen late in pregnancy, and he suggests that it may represent a very advanced degree of porencephaly.

The description of this case is illustrated by three very good photographs of the external view of the head and both halves of the sections of the head after hardening, with the structures *in situ*.

Congenital Lacunar Skull.

Bettinger describes the case of a primipara aged 20 years delivered of a female child at the eighth month of pregnancy. The child had a spina bifida in the lumbar region and marked bilateral talipes. The child survived 7 days and during this time it developed a steadily increasing tension of the fontanelle and signs of inflammation of the spina bifida.

On post-mortem examination except for the presence of a horse shoe kidney abnormalities were confined to the skeleton. The feet were in extreme talipes and in addition to the spina bifida in the lumbar region there was a sharp-angled kyphosis in the same region. The skull was the site of the most striking abnormality. After removal of the scalp a large number of slightly bulging areas was seen. These were covered only with a thin membrane and no bone. A number of these areas were oblong shaped and arranged symmetrically on both sides of the mid line in the parietal bones and more irregularly in the frontal and occipital bones. On removal of the vault of the skull the areas appeared as deep cavities lined by thick smooth ridges of bone. The convolutions of the brain were flattened to correspond to these depressions. After removal of the brain a gross exaggeration of the configuration of the base of the skull was seen. All the grooves were deeper and all the ridges more prominent than usual but the condition was less marked than in the vault. A horizontal section through the brain showed a considerable degree of hydrocephalus.

After giving a short résumé of all the theories that have been advanced to account for the occurrence of lacunar skull the writer concludes that the following explanation is correct.

Towards the end of pregnancy there is non-physiological incongruity between skull and brain. Under normal conditions localized incongruities do not occur because the cerebrospinal fluid acting as a water cushion ensures an equal pressure upon all parts of the cranium. In the case of a meningocoele the escape of cerebrospinal fluid into the sac allows the brain to come into direct contact with the inner surface of the vault. Additional space for the growing brain cannot be obtained by bulging of the non-osseous parts of the cranium because the surrounding amniotic fluid does away with all pressure differences. Erosion of the bone by pressure atrophy will therefore occur wherever the gyri press most closely against the inner table. A typical lacunar skull will then develop.

Granulosa-cell Carcinoma of the Ovary, with the Report of a Case.

Mackey reports the case of a single woman of 32 years complaining of bleeding *per vaginam* for 6 months. The periods started at 13 years, had always been irregular and accompanied by dysmenorrhoea. Three years before, at the age of 29 years she started a period of amenorrhoea which lasted two years followed by irregularity for one year.

On examination blood was found to be coming from the cervix, the uterus was slightly enlarged

and a freely movable tumour the size of a foetal head could be defined in the posterior fornix. In view of the patient's oestrogenic disturbance a diagnosis of granulosa cell tumour of the ovary was made and this diagnosis was confirmed at operation.

The macroscopic and microscopic features were typical. R. H. B. ADAMSON

American Journal of Obstetrics and Gynecology

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*The effects of analgesia on the newborn infant. C. O. McCormick.

A report on a series of complete tears of the perineum with extension up the posterior vaginal wall, repaired by the vaginal flap method. R. E. Campbell.

Acidosis and alkalosis in obstetrics and gynaecology. W. T. Pride, J. R. Reinberger and D. T. Holland.

Home delivery service for medical students. C. R. Hannah.

Nationality and carcinoma of the cervix. F. R. Smith.

*A skin test for the diagnosis of pregnancy. F. H. Falls, V. C. Freda and H. H. Cohen.

Objections to induction of labour in normal pregnant women. E. L. Cornell.

Pubertas precox due to ovarian tumours. C. B. Lull.

Actinomycosis of the ovary. W. A. Coventry.

The treatment of pelvic endometriosis. W. T. Dannreuther.

The effect of combined administration of chorionic gonadotropin and the pituitary synergist on the human ovary. C. Mazer and E. Ravetz.

A comparative study of male and female pelves in children, with a consideration of the aetiology of pelvic conformation. D. G. Morton and C. T. Hayden.

Some observations on the gynaecic employment of equine gonadotropins. E. C. Hamblen.

Menstruation and urination through a clitoris-like structure. D. N. Barrows and W. N. Bloch.

Amenorrhoea and sterility caused by bilateral polycystic ovaries. M. L. Leventhal.

Meigs' syndrome. F. R. Lock and C. G. Collins.

Fulminating systemic haemolysis following incompatible blood transfusion. M. Fellman.

Dermoid cyst of the ovary with squamous cell carcinoma. S. Brody.

Herpes gestationis. S. J. Turner and S. J. Zakon.

Diabetes insipidus complicating pregnancy. S. D. Hart and H. B. Breitman.

A study of puerperal mortality in New York City (1937-1940) with especial reference to preventive factors. R. G. Douglas.

Puerperal mortality in the Borough of Brooklyn, City of New York. C. A. Gordon.

Society transactions.

Selected abstracts. Ectopic pregnancy.

THE EFFECTS OF ANALGESIA ON THE NEWBORN INFANT.

McCormick says that no single issue divides obstetricians so much as that relating to the use of analgesia; some do not use it and criticise it severely, while others use it and praise it loudly. One of the main arguments against its use is its supposed bad effect on the child. Those who use it maintain that this supposition is erroneous, although there is no doubt that it does cause some delay in the initial respiration, and yet no proof for or against this statement has been forthcoming. In this paper the author does bring forth evidence, not only that it is harmless to the child, but also that it is actually beneficial. Investigators, previous to the writing of this paper, had found that the stillbirth and neonatal mortality-rates had decreased during the period of barbiturate administration. Some also found that the infants lost less weight and gained weight quicker when the labour had been conducted under analgesics. It has been suggested that the "physiologic weight loss" might be more than just physiologic and perhaps is a direct index of the amount of shock sustained. Apart from this amount of weight loss and this rate of weight loss recovery, there was a tendency for the babies born under the influence of drugs

to maintain a more normal temperature for the first 10 days of life. These findings become all the more interesting when it is realized that the percentage of low forceps is high when the labour is conducted under some form of analgesia. One would expect an operative delivery itself to have a deleterious effect on the infant and that this might be enhanced by the analgesic used.

As the result of these accounts in the literature and of his own investigations, the author is of the opinion that there is a high degree of general safety for the newborn when the mother is delivered under many of the modern varieties of pain-relief. He thinks that opiates are probably the only analgesics that may materially affect the infant adversely and may be particularly hazardous in cases of prematurity.

A Skin Test for the Diagnosis of Pregnancy.

As skin reactions have been used as an aid to clinical diagnosis of many conditions, the authors were of the opinion that a skin reaction to some antigen might be obtained to distinguish pregnant and non-pregnant individuals. One of them had extracted a protein from the placenta many years ago but it was not satisfactory because of the difficulty in getting it sufficiently refined. Since then other workers have made placental extractions but the intradermal reaction was positive in only 75 per cent of pregnant women but negative in the non-pregnant. In this paper, they describe their results after the injection of colostrum into the skin. The material was obtained by expression after cleansing the nipple with ether and it was diluted with an equal amount of sterile normal saline solution. The injection was made into the flexor surface of the forearm and a weal was formed by injecting exactly 1/50 of a c.c. A similar sized weal was made with physiological salt solution, a few inches lower, as a control. After about 30 minutes the weal would appear pearly, with little or no pinkish areola around it, if the patient was pregnant. If the patient was not pregnant, the weal would remain pearly for a few minutes and then would begin to increase in size, eventually becoming two or three times the size originally produced by the injection, without changing in colour. Then there would appear a pinkish-red areola, one or two inches in diameter, which was irregular in contour and in depth of colour. This reaction would grow in intensity for an hour and persist for four or five hours.

The authors injected 265 known pregnant women in various stages of pregnancy, 358 known non-pregnant cases, including adult males, children, menstruating women, normal non-pregnant women, and women with known gynaecological abnormalities, and 50 unknown problem cases to establish diagnosis. Of the 265 known pregnant women, there were five false reactions. Two non-pregnant reactions were obtained, one of which later gave the reaction for pregnancy and the other was not repeated. Three weak non-pregnant reactions were also obtained but disappeared after an hour, contrary to the usual non-pregnant reaction. It was also found that very early in pregnancy and during labour that there was a tendency to get a weak non-pregnant reaction which did not persist. Of the 113 known non-pregnant females, four cases gave a typical pregnant reaction. These were all in the menopause, not having menstruated for five to 17 years. Of 50 post-partum cases, varying from two to eight weeks after delivery, all but three gave a non-pregnant reaction. Thus the test was correct in 98 per cent of pregnant women and in 96 per cent of non-pregnant women. Children before puberty reacted similarly to pregnant women.

From these experiments the authors came to the conclusion that the failure of the pregnant woman to react to the injection is due to an immune state which prevents the local reaction at the site of the injection; the weak reaction, seen in about 80 per cent of the cases in the first six and last three weeks of the pregnancy, during labour, and in the early days of the puerperium, is the exception. The specific protein contained in colestrum from primiparous women is not contained in human milk or in colostrum or milk obtained from the cow, as no specific reactions were obtained with these substances.

REPORTS OF SOCIETIES

THE ROYAL ACADEMY OF MEDICINE IN IRELAND.

A meeting of the Section of Obstetrics was held on Friday, November 20th, 1942.

Dr. BETHEL SOLOMONS showed

A SPECIMEN OF PLACENTAL POLYPUS.

The patient was aged 36; she had had 11 children, the last 11 months previously. She was admitted to the hospital in September, 1942. She had nursed her baby; menstruation has recommenced 4 months ago. Since July bleeding has been more or less continuous. Examination revealed a rather soft, slightly enlarged, uterus. She was in such a collapsed state on admission that it was decided to give her a blood transfusion. As a temporary measure she was given intravenous saline and the uterus was plugged. Owing to her condition it was decided that conservative measures would be dangerous, and total hysterectomy was done. The pathological report by Dr. Bourke was as follows:

"*Tumour*: This is a simple placental polypus with necrotic chorionic villi all through it. At one or two places on the surface the villi appear to be covered with living cells. The endometrium in the roughened area above the polypus shows much blood in the interstitial tissue, with large areas of hyaline degeneration around the blood-vessels. There is also evidence of early adenomyosis."

Dr. BETHEL SOLOMONS said that when he got the report he believed the condition was very rare; in fact, it was one of those conditions that he had taught about, but had seldom seen. He could find no records as to its frequency. The appearance of the specimen which he showed was consistent with the description of Novak: he suggests that profuse haemorrhage may occur from rupture of the large venous sinuses at the base of the polypus: and he recommends the pathologist to take care to make a differential diagnosis from chorionepithelioma. In this case no history could be obtained of a definite abortion, nor of retained placenta at the last birth.

Dr. D. J. CANNON showed

A CASE OF UTERINE PLACENTAL POLYPUS,

which was associated with severe bleeding, so severe that a blood transfusion had to be administered prior to operation. Curettage revealed normal endometrium. When the uterus was split after supra-vaginal hysterectomy, the appearance of the polypus so closely resembled that of a malignant polypus that he decided to remove the cervix and both ovaries. The patient made an uneventful recovery. The polypus showed microscopic evidence of chorionic villi.

Dr. CANNON also showed

TWO FALLOPIAN TUBES ASSOCIATED WITH A CHOCOLATE CYST OF THE LEFT OVARY.

The Fallopian tubes showed a deposit of fat globules and fatty acid crystals in the submucosa. This was apparently a metabolic change due to some unknown cause.

Dr. JAMES QUIN showed

A SPECIMEN OF UNILATERAL CHRONIC SALPINGITIS.

He said he considered it interesting as the size of the Fallopian tube was unusual, and the condition unilateral.

The patient was aged 51, a widow, without children. She suffered from vague abdominal discomfort and evening rise of temperature. The symptoms were not acute, but tenderness and pain were mainly referred to the back and left side. In spite of her age her periods were quite regular until about 6 months ago. She had 6 months of amenorrhoea of menopausal type and then had severe bleeding with clots, which lasted 5 days. A large mass was felt on the left side of the abdomen, extending above the umbilicus; it was smooth; and some mobility and tenderness were noted. Rectal examination revealed an impacted mass in Douglas's pouch. Further examination showed that the cervix had no signs of erosion or carcino-

matous change, but there was a cystic mass in the right fornix. The uterus appeared to be enlarged. A diagnosis of ovarian cyst with possible fibroids was made and the abdomen was opened. Operation revealed a huge left pyosalpinx full of fluid and enormously distended. The uterus was enlarged and soft. The right Fallopian tube was merely thickened. The uterus was removed with both ovaries and Fallopian tubes, after having first removed the left Fallopian tube separately. Both ovaries were apparently normal. The vagina was left open for drainage. The pathologist reported "a huge pyosalpinx filled with straightforward polymorphonuclear pus." The tubal condition was a chronic pyosalpinx, and not tuberculous.

Dr. QUIN went on to say that it is obviously not an acute condition, he did not know why a unilateral salpingitis of this nature should arise, and would be interested to hear any comments on the matter. The uterus was large and thickened without any definite pathological condition other than that which one would associate with chronic congestion. The other Fallopian tube was thickened and hard; it contained no pus.

The PRESIDENT, DR. NINIAN FALKINER, Master of the Rotunda Hospital, said they had all been interested to see these specimens; with regard to the question of placental polypus, he thought the first unessential cause to be partly retained placental tissue following confinement. He thought it fairly common for part of a placenta to remain *in utero* without being recognized at the time. It may give rise to haemorrhage, and during the treatment the placental tissue may be removed. A number of patients go through a period without undue loss and afterwards placental polypi develop. Chorionic tissue becomes absorbed but the blood-vessels at the base of the cotyledon seem to remain in the same position.

He said he would like Dr. Solomons to say how long after delivery his patient came for treatment. Dr. Cannon stressed the point of diagnosis at operation; but surely diagnosis in these cases should be made not when the abdomen is opened, but by curettage. It is quite easy, as a rule, to get a bit of the polypus and the presence of villi would disclose the diagnosis at once; the pathologist would have no difficulty in stating if the villi were, microscopically, those which are found in chorionepithelioma. He had very little to say about the condition of the Fallopian tubes in Dr. Cannon's case, except that there is a great deal of fat in the corpus luteum. With reference to the chocolate cyst, he said he was not clear whether it was endometrium or cyst filled with blood.

Referring to Dr. Quin's specimen, the President said it was one of the largest Fallopian tubes he had ever seen. The only explanation as to its size is, that at the same time this Fallopian tube had become twisted and had a haemorrhage into it, which had gradually become absorbed; that suppuration had taken place and when the Fallopian tube was removed all sign of haemorrhage had disappeared. Was the condition of the Fallopian tube recognized at the time of examination which would suggest that there had been a haemorrhage, and had there been a remote history of acute abdominal illness and recovery without operation.

Dr. J. F. CUNNINGHAM said he had seen cases similar to those shown. The reason for the lack of statistics of placental polypus was that it was such a rare condition. He said he thought he had seen one case 5 months after delivery, and went on to describe the symptoms and treatment he had given for the severe bleeding; he performed total hysterectomy, and gave a blood transfusion. On examination the uterus was empty. There was a large sinus present.

Dr. Cunningham said he was also interested in the large Fallopian tube shown by Dr. Quin. He had seen a case with a pelvic abscess; he opened Douglas's pouch, but no pus was found. He felt a cystic mass and found the right Fallopian tube very distended; the left Fallopian tube was normal. He stated that it was hard to explain the condition of salpingitis. There were no adhesions in his case.

With reference to Dr. Cannon's case he said he could not offer any explanation to account for fat globules being deposited there.

Dr. J. O. E. APTHORP asked Dr. Solomons and Dr. Cannon did they not think the term uterine polypus wrong and misleading? Both cases showed evidence of actively growing tissue. If a bit of placenta is left behind it is no different from any other foreign body; therefore, it is not actively

growing. He suggested that the term should be changed.

With regard to Dr. Quin's case both Fallopian tubes showed chronic inflammation: Would the end result depend on whether the Fallopian tube became sealed off. Why should one become sealed off and one not?

Dr. E. SOLOMONS also spoke.

Dr. Bethel Solomons, in reply to various questions, said if there was any doubt as to malignancy, total hysterectomy should be done. He suggested that polypus was a better word than polyps. Curettings might easily be negative as they were in his case.

The last baby was born 11 months previously; the patient lactated for 7 months and then the bleeding started and was nearly continuous.

Dr. Cannon, in reply to questions, said that the uterus was curetted in his two cases and both were negative. Therefore, he considered it very difficult to make a diagnosis by curettage. He treated the first case by supravaginal hysterectomy; the second case by total hysterectomy.

There was, according to Dr. O'Kelly, no evidence of inflammation of the Fallopian tubes in the second case.

Dr. Quin also replied.

Dr. J. F. CUNNINGHAM read a paper,

ON THE TREATMENT OF ECLAMPSIA

and reported 105 cases from the National Maternity Hospital. He stressed the importance of attention to the condition of the kidneys, the liver, the cardiovascular system and the amount of oedema present. He made special reference to the use of magnesium sulphate in treating eclampsia, and produced figures showing a diminution in the mortality-rate and in the number of fits under this treatment. He drew attention to the importance of an accurate history as a help in determining the presence of a previous lesion in any vital system. He pointed out that most of the fatal cases occurred in those who had neglected prenatal care.

The PRESIDENT thanked Dr. Cunningham for bringing this communication before the Academy and remarked on the decreased mortality-rate of maternity cases. He thought half the deaths were due to the toxaemias of pregnancy. He said that in the Dublin maternity hospitals there have been an average of 10 to 12 deaths in a period of 7 years from eclampsia. Dr. Cunningham's figures bore that out; they also show that, since the establishment of the routine use of magnesium sulphate and highly concentrated glucose solution, combined with careful observation and nursing, the death-rate from eclampsia would probably be reduced by 50 per cent. He was interested to hear of the histories of the fatal cases and agreed with Dr. Cunningham that if these cases had received antenatal care the result would have been different. He congratulated him on the treatment of 105 cases of eclampsia and particularly on the results of the last 50 cases.

Dr. BETHEL SOLOMONS said he was glad to take this opportunity of paying tribute to the excellent work which Dr. Cunningham had done for the Dublin School of Midwifery and for the National Maternity Hospital.

The subject of eclampsia had always interested him and he had brought 204 cases with a mortality of 8 per cent, treated during Dr. Tweedy's mastership, before the British Congress of Gynaecologists in Liverpool. Of these cases 30 occurred during the last 2 years of the mastership when Dr. Freeland and he were assistants, when there was no mortality. He thought it would add to the value of the excellent paper if, in dealing with the 119 cases in the first series, it were stated how many received prenatal care.

Dr. CORBET congratulated Dr. Cunningham on his communication and congratulated him on the excellent results achieved in his last 50 cases. He thought that the real significance in the treatment was not, perhaps, so much the reduction which appeared in the mortality-rate, but in the control of the fits, as shown by the very small percentage which occurred after treatment had started. He agreed with Dr. Cunningham on the importance of dehydration and had used this method since its publication by Fay and Arnold in 1932. He had used magnesium sulphate on only a few occasions, as he had found great difficulty in obtaining the required solution in ampoules. He did use, as long as he had been able to obtain it, the 50 per cent solution of glucose for intravenous injection, and

he did not find that it invariably caused a rise in blood-pressure although, in some cases, it certainly caused a rise in the tension of the cerebrospinal fluid.

He used lumbar puncture almost as a routine, and was satisfied that some cases benefited greatly from it. One patient, who had haemoglobinuria, a sign which previous experience had always led him to believe of fatal import, showed immediate improvement on lumbar puncture and eventually recovered. He used venesection only when there were signs of embarrassment of the right heart; occasionally, in these cases, a dramatic result was produced.

Dr. Corbet quoted statistics compiled from collected hospital reports of English, Scottish and Colonial institutions. The totals for these institutions showed a variation in the incidence from 5.7 per cent of admissions for Trinidad to 0.3 per cent of admissions for Hong Kong. The mortality-rates varied from 16.3 per cent to 12 per cent.

The incidence-rate at the Coombe Hospital was 5.3 per cent and the total mortality-rate 12.5 per cent.

Dr. QUIN congratulated Dr. Cunningham on his results. In comparing his figures with previous Dublin figures, particularly Dr. Tweedy's, it must not be forgotten, he said, that in those days there was a completely inadequate system of antenatal treatment, and therefore there must have been a number of patients who would never have developed eclampsia with our present antenatal treatment. Therefore, the mortality statistics then would be actually less than now.

He asked Dr. Cunningham about the value of lumbar puncture when cerebral symptoms were marked. He stated that he considered gas and oxygen anaesthesia an improvement on chloroform. With regard to gastric lavage, he looked on it as unnecessary.

Dr. R. W. SHAW discussed the question of anaesthetics. He said he would like to ask Dr. Cunningham if he was able to use pure gas and oxygen in these cases. It would appear that many of these cases must have been extremely difficult for any anaesthetic. In his experience he found, even in emergency cases of abdominal section, the administration of gas and oxygen alone a peculiarly difficult one unless the patient was adequately prepared. He also asked if Dr. Cunningham considered that the administration of ether or chloroform definitely adds to the risk or whether he considered that, if there is difficulty with gas and oxygen, it would be better to give a pure ether anaesthetic.

Dr. A. W. SPAIN, Master of the National Maternity Hospital, said what impressed him most when he took up the mastership from Dr. Cunningham, was the organization of the treatment of cases of eclampsia when they came into the hospital. He had no change to make and the treatment with magnesium sulphate was still used. It was too soon to give the number of cases of eclampsia since he took up the mastership, but it has been small; he had one in the first 6 months, and then 7 or 8 cases. Dr. Spain said he used gas and oxygen and found it ideal in cases of eclampsia. He had performed one Caesarean section under local anaesthesia. Three hours before the operation he thought the case was hopeless and at that stage did a lumbar puncture. She then showed some slight improvement and he did the Caesarean section.

Dr. Spain said he hoped to continue Dr. Cunningham's line of treatment with magnesium sulphate. He considered it would be better to avoid morphia.

Dr. E. SOLOMONS congratulated Dr. Cunningham on his results. He said he would like a few details about submammary, intravenous and intramuscular injections. Had he ever seen any bad results, or any local bad effects follow such injections? He asked him if there was any scope for the use of magnesium sulphate in other severe toxaemias.

Dr. F. Cunningham thanked the President and Section and the various speakers for the reception of this paper and the complimentary things said about it. He said he had studied Dr. Tweedy's remarkable success in the treatment of eclampsia. He considered that the long distances which eclamptic patients had to travel by car nowadays had a very bad effect, and that in Dr. Tweedy's day long journeys by car were not so frequent; the same thing would apply to Dr. Corbet's statistics.

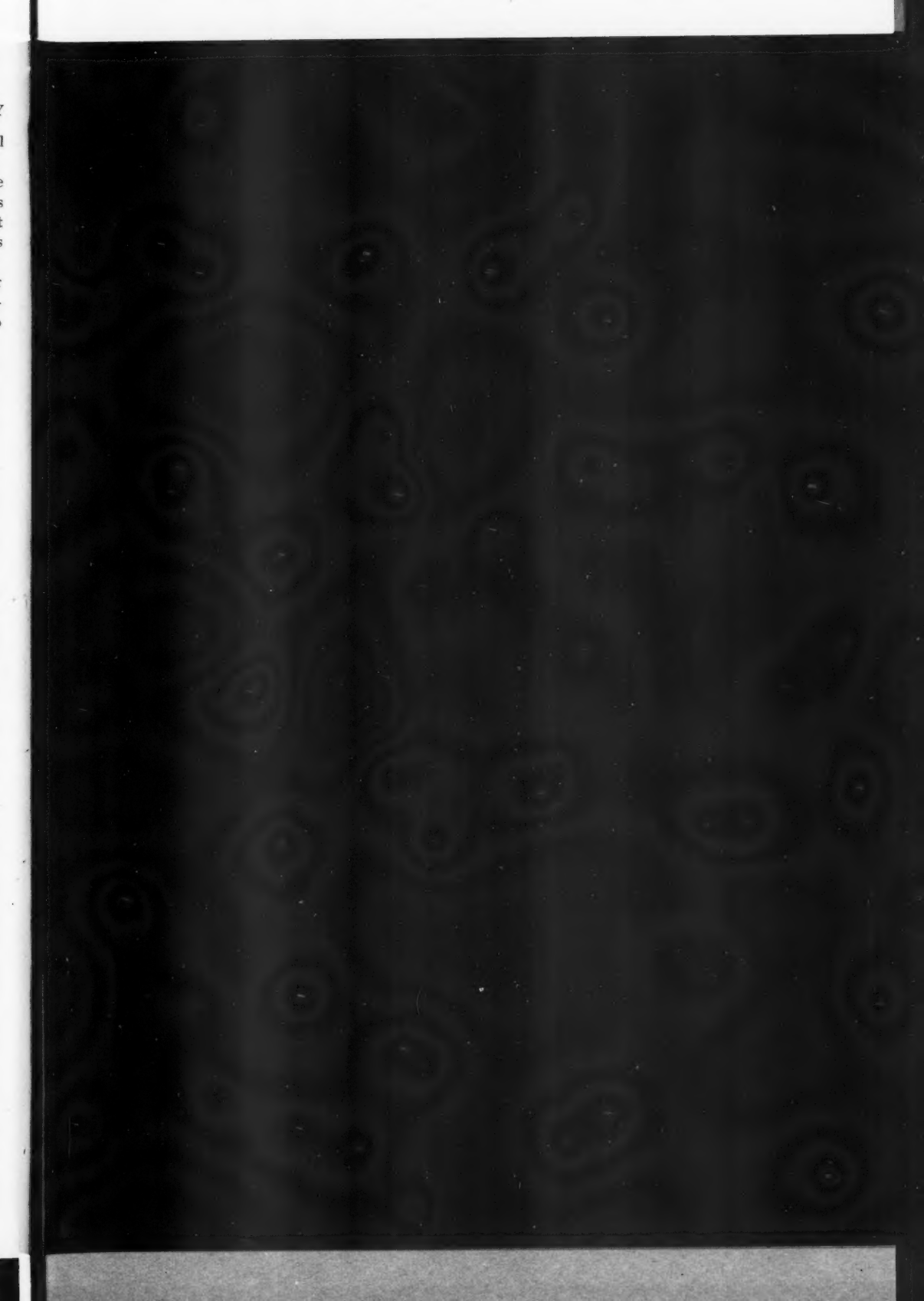
As regards liver tests, he did the Vanden-

burg test only, as there is not time for others in acute eclampsia. The function of the kidneys is tested by estimation of the blood-urea. Magnesium sulphate is given early when the blood-pressure is inclined to rise; if given with the glucose it did not rise. He said he considered that magnesium sulphate, if given in the beginning, is a great help. Lumbar puncture was not done as a routine when one can give the patient a concentration of glucose. It is done in a patient in whom there is a good deal of restlessness and nasal itching, with good results, and when the patient gets strong solutions of glucose. The mortality-rate in eclampsia depends on the type of case, whether they had had prenatal care or not.

He went on to say that there must be a place for Caesarean section in eclampsia, but it was difficult to make up one's mind when a patient is in labour with eclampsia. The general results with Caesarean section were very bad.

Dr. Cunningham said he never gave any other anaesthetic but gas and oxygen. He gave a maximal dose of a quarter of a grain of morphia. No patient had more than 1 grain during 24 hours.

He gave injections intravenously and intramuscularly.



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